TRANSACTIONS

AMERICAN ACADEMY of OPHTHALMOLOGY and OTOLARYNGOLOGY

JANUARY - FEBRUARY
1958

Volume 62 No. 1

ANNUAL MEETING, OCTOBER 12-17, 1958, CHICAGO

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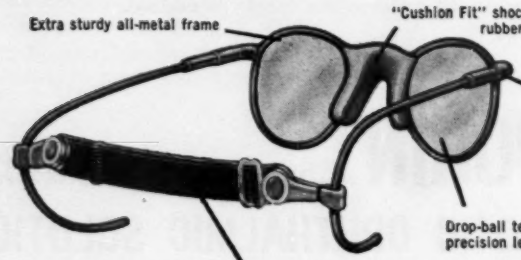
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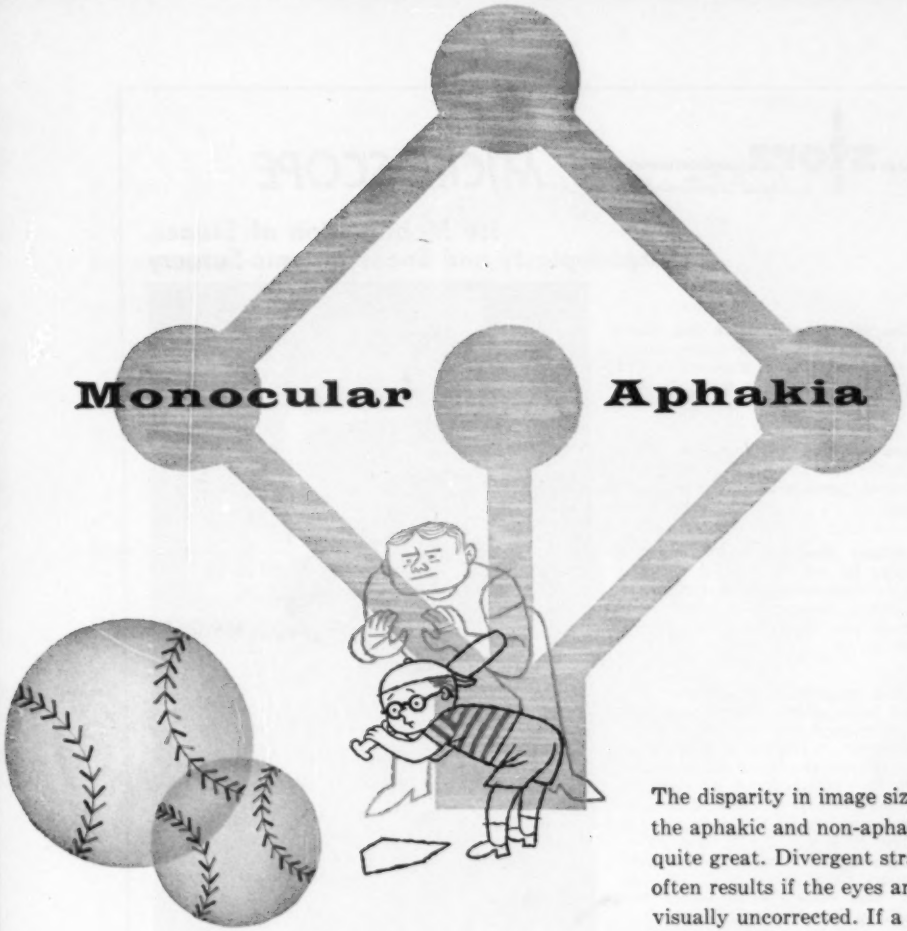

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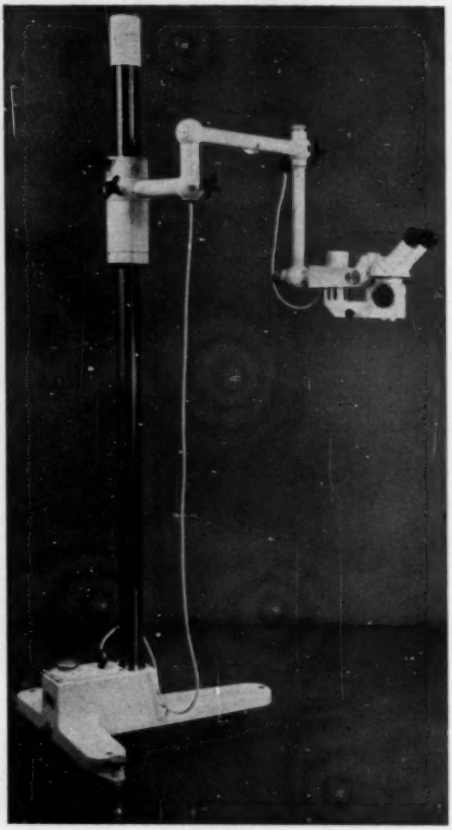

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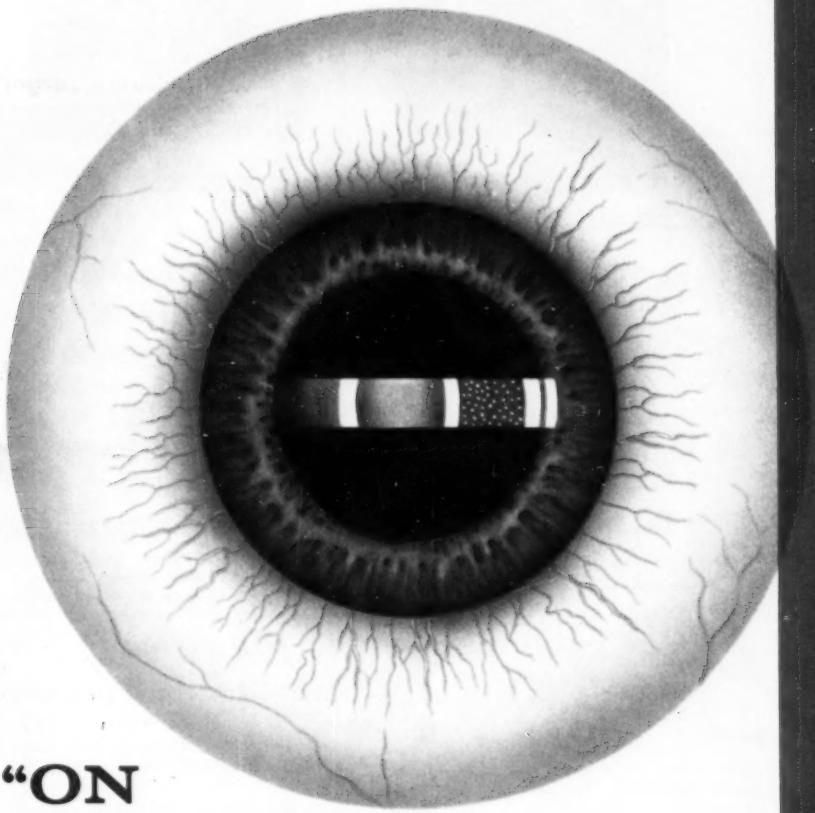

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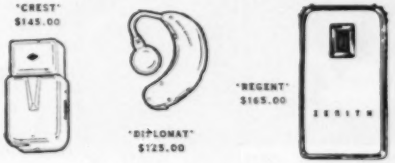

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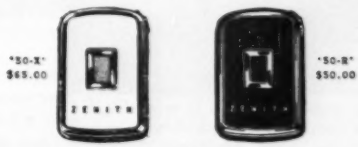

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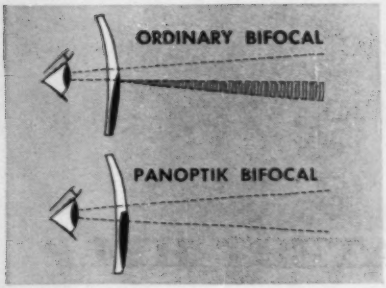

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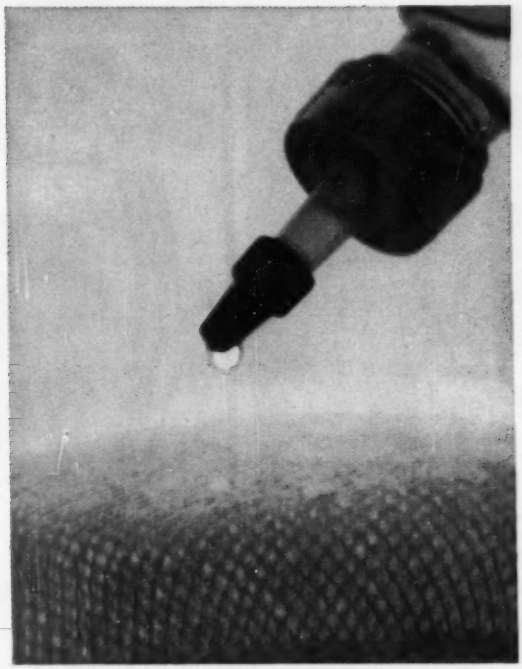

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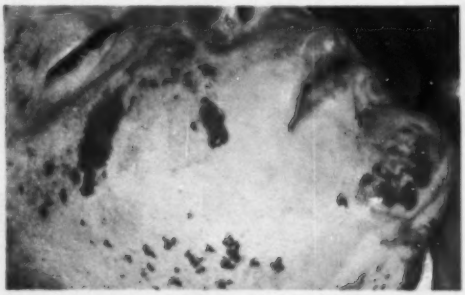

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Case #2 Left cheek untreated

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1. *Dripps, R.D.: Hazards of the Immediate Postoperative Period, J.A.M.A. 7:795 (Oct. 19, 1957) [This reference reviews postoperative hazards, and does not refer to Adrenosem Salicylate]*
2. *Ersner, M.S., and Lerner, S.S.: M. Clin. North America 40:1749 (Nov., 1956)*
3. *Peele, J.C.: Further Observations on the Use of Adrenosem Salicylate in the Control of Hemorrhage from the Nose and Throat, N. Carolina M.J. 17:98 (March, 1956)*
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7. *N.N.R., 1957, p. 265*

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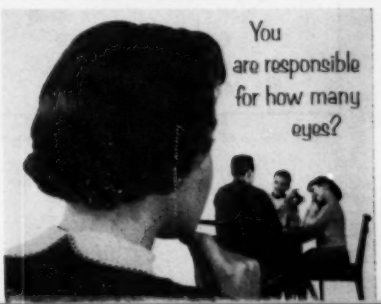

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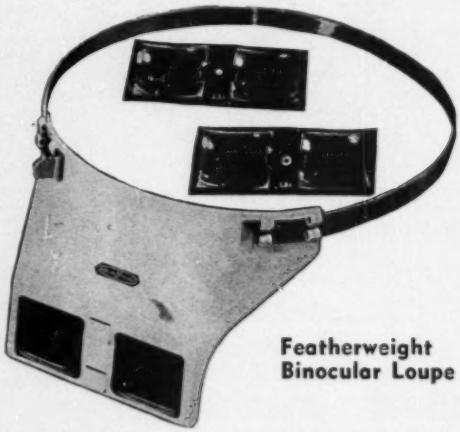

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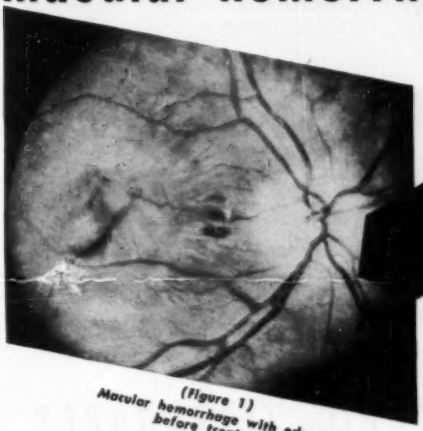
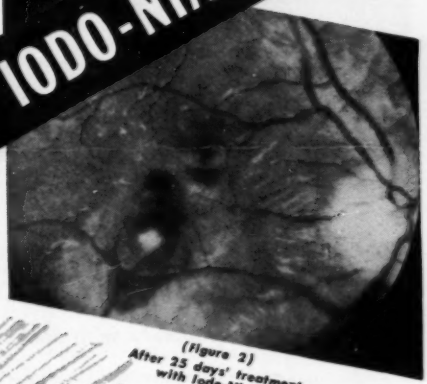


(Figure 1)
Macular hemorrhage with edema, before treatment



(Figure 2)
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1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.
4. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1598.

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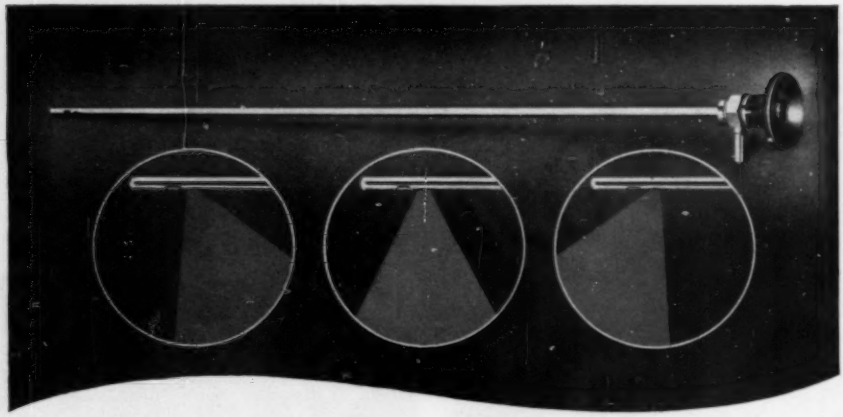

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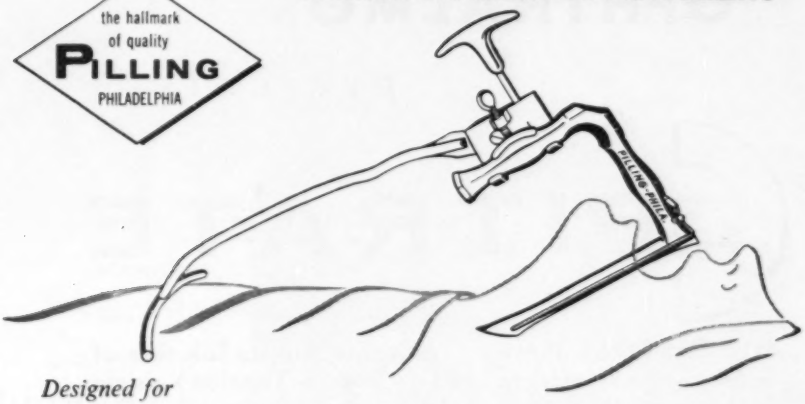

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Reference—R. B. Lewy: Acta Oto-Laryngologica, Vol. 46, Fasc. I, 1956

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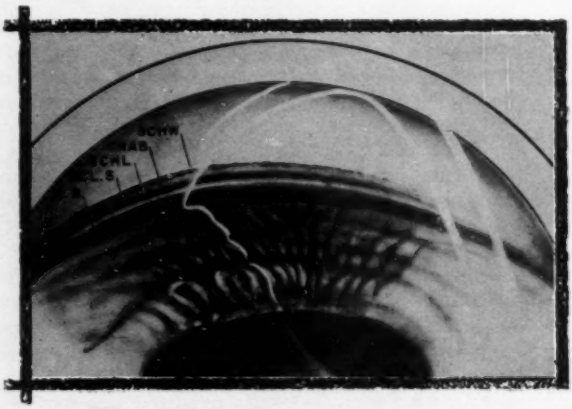

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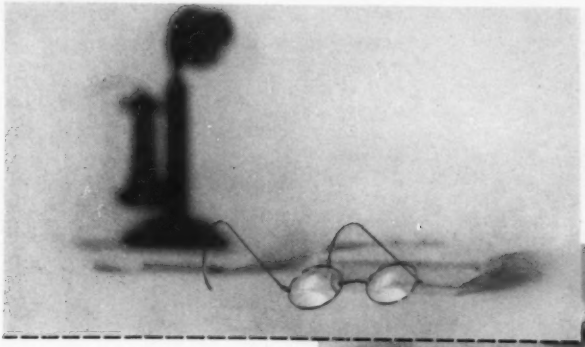

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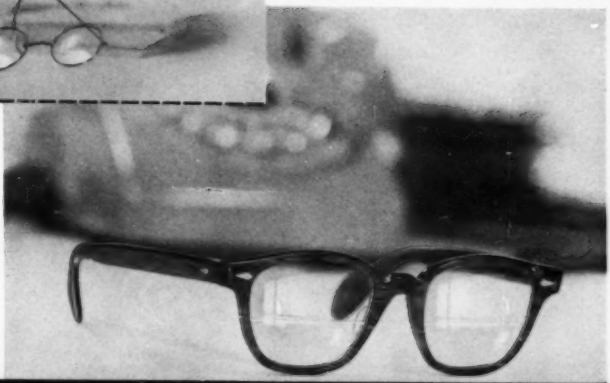

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1. Rasgorshek, R. H. and McIntire, W. C.: Am. J. Ophth. 40:34 (July) 1955. • 2. Ehrlich, L. H.: N. Y. State J. Med. 53:3015 (Dec. 15) 1953. • 3. Gettes, B. C.: A.M.A. Arch. Ophth. 51:467 (April) 1954. 4. Council on Pharmacy and Chemistry: J.A.M.A. 158:1523 (Aug. 27) 1955. • 5. Stolzer, I. H.: Am. J. Ophth. 36:110 (Jan.) 1953.

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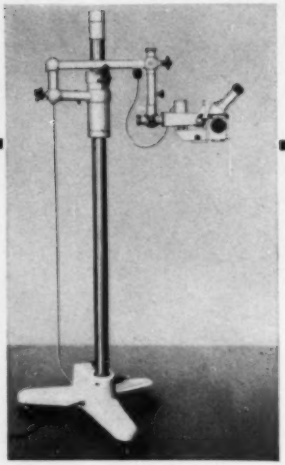

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XIV Jackson Memorial Lecture

OCULAR TOXOPLASMOSIS

MICHAEL J. HOGAN, M.D.
SAN FRANCISCO, CALIFORNIA

IT is an unusual honor to be invited to present this lecture in honor of Dr. Edward Jackson. Fortunately I knew him for a few years before he died. Even at his advanced age it was obvious that he was a man of great simplicity and good humor, and that he possessed an active and inquiring mind. He was constant in attending meetings, and we encountered Dr. Jackson frequently at meetings on the Pacific Coast. At that time my wife worked in her father's [H. G. Merrill, M.D.] office. At these meetings he delighted in discussing basic problems and perplexing her with unusual refractive and muscle problems.

I asked some of Dr. Jackson's associates for reminiscences about his days in Denver and at various meetings. Many of them dealt with his ability as a teacher, his devotion to ophthalmology, and the manner in which he made Denver a mecca for ophthalmologists. Apparently he was unostentatious, dressing and practicing in a very simple manner. His office was not ornate, and I was informed that it was common for him to make house calls on a bicycle or in a model T Ford.

One of the best tributes came from one of his former pupils, Dr. Phillips Thygeson, and I have asked permission to quote him verbatim:

> It was wonderful knowing Dr. Jackson. He was not only one of the ablest but one of the gentlest and kindest men that has ever graced our profession. I wish I had the words to put over a little of his flavor and charm and essential goodness.

Introduction

Human toxoplasmosis is one of the most interesting diseases of modern medicine. Its manifestations are protean and, in the acquired form, resemble those of a number of well-known disease entities. At first glance it is surprising that diagnostic studies have failed to show the frequency of this disease. However, one of the important diagnostic tests, the methylene blue dye test, is technically difficult and involves the risk of handling live organisms. These factors probably have restricted widespread testing and have prevented more rapid progress in the diagnosis of the disease. The evolution of our knowledge of this disease has followed the pattern usually observed in infectious diseases; it was first discovered in various animals and birds, and many years later in humans. The eye manifestations of this disease are important and have been subjected to considerable study. It is important at the present time that the entire subject be reviewed, and that additional information be presented with regard to ocular involvement.

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I wish to express my thanks and appreciation to Miss Ann Lewis and Mrs. Phyllis A. Zweigart for their assistance in conducting these studies and in preparation of this paper.

Presented at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

In 1908 Nicolle and Manceaux[25] reported the finding of organisms similar to Leishmania in a North African rodent, the Gondi. They found the organisms to be widespread in the tissues, but, unlike Leishmania, the kinetoplast was absent. In the following year these authors gave the organism the name Toxoplasma.

Since publication of these reports, spontaneous Toxoplasma infections have been observed and reported in a wide variety of wild and domestic animals and birds, including those used for experiments in laboratories. In a number of instances different names were assigned to the strains isolated from various species, but studies soon verified the fact that all were members of the same species. All strains appear to be serologically and biologically identical but differ considerably in their virulence.

It was not until 1938, however, that Wolf and his co-workers[43] discovered toxoplasmosis in man. They reported the isolation of Toxoplasma from a 31-day-old infant who developed an acute and fatal illness within a few days of birth. Clinically this infant suffered severe encephalomyelitis and bilateral chorioretinitis. These findings were verified at autopsy. Toxoplasma organisms were observed in microscopic sections and isolated from experimental animals which were inoculated with the infant's tissues. This study also was the first to show that an apparently healthy mother could give birth to an infected infant.

Following the study of Wolf and his co-workers, many reports of congenital toxoplasmosis were published. Most of these reports indicated that lesions of the eye, the central nervous system, and the viscera were common.

Although congenital toxoplasmosis has been considered in the past to be a rare disease, there now is evidence that many infants are born with unrecognized infections. The congenital nature of the infection may be discovered only in those cases where a later flare-up occurs.

It was suspected by many for a number of years that some forms of chorioretinitis in older children and adults might be due to acquired types of toxoplasmosis, but methods to prove this were lacking until the discovery of the toxoplasmin skin test in 1947[13] and the methylene blue dye test in 1948.[32] The dye test is based on the principle that antibodies in the patient's serum are able to prevent live Toxoplasma from staining with methylene blue (table I). A substance in fresh normal human serum, probably properdin plus complement fraction, known as accessory factor, is necessary to accomplish this reaction. The highest dilution of serum in which over 50 per cent of Toxoplasma are unstained is the end point.

By using the skin test in population surveys it was demonstrated that there was an extremely high incidence of toxoplasmic infections throughout the world. Feldman and Sabin[12] first showed that the incidence of positive skin tests rose

TABLE I

PRINCIPLE OF THE METHYLENE BLUE DYE TEST

Antigen	+	Antibody	+	Accessory Factor
(Organisms from Mouse Peritoneal Fluid)		(Patient's Serum)		(Fresh Normal Human Serum)
Methylene Blue Fresh 20%, pH 11	→	Heated at 37°C one hour	→	Over 50% of Organisms with Unstained Cytoplasm

from 5 per cent in persons in the age group from 5 through 9 years to 50 per cent in those in the age group from 30 through 40 years, and to 65 per cent in those over 40. With minor variations other observers confirmed this finding in the United States and European countries. Subsequent studies with the dye test supported these findings.

It is my intention to review some of the important advances in our knowledge of toxoplasmosis, the epidemiology of the disease, its diagnosis and treatment. Emphasis will be placed on the results of our studies in the diagnosis and treatment of the ocular form of this infection.

Biology of Toxoplasma

Toxoplasma is classified as a protozoan parasite. It is an obligate intracellular organism which reproduces by longitudinal fission within a host cell or in its vicinity. It measures 4 by 7 microns and is crescentic in shape in its extracellular form. Within cells and after fixation it is somewhat rounded. Prolonged survival in tissues leads to formation of pseudocyst forms in which numbers of organisms are surrounded by a capsule which stains with silver.

Toxoplasma does not withstand drying, freezing, and ordinary chemical action. In Tyrode's solution or in mouse peritoneal fluid it can survive up to four weeks at ordinary refrigeration temperature. It can be grown in animals, eggs, or tissue culture. A wide variety of cells can be used to maintain the organisms in tissue culture, although the yield of organisms is usually low.[20]

Toxoplasma is pathogenic for a large number of mammals and birds. It can be propagated by direct transfer of infected tissues or fluids into healthy animals, cell cultures, or fertile eggs. Infection of animals can be achieved by inoculation of organisms by any route. A parasitemia follows growth at the site of inoculation and persists for a variable period, depending on the host, the virulence of the Toxoplasma strain, and the numbers introduced. Antibody formation results and can be detected at a suitable interval after the inoculation. The organisms spread throughout the body but seem to prefer the tissues of the central nervous system, where they may persist for years. This persistence also occurs in the eye, for we have demonstrated that organisms can be recovered from the chorioretinal tissues up to two years after inoculation into the vitreous of the eyes of guinea pigs.[19]

Epidemiology

Skin tests, and serologic and cultural studies in man, birds, and animals (wild and domestic) have shown that toxoplasmosis is frequent and widespread. Sporadic cases and epidemics have been reported from practically all portions of the world. Feldman and Miller[11] studied ten human and twenty-four animal populations with the methylene blue dye test. There was a low incidence of positive tests in Eskimos, Navajo Indians, and Icelanders. In various urban populations in the United States, 17 to 35 per cent of the sera were positive at titers of 1:16 or above. A higher incidence of positive tests at 1:16 or over was found in Haiti (36 per cent), Honduras (64 per cent), and Tahiti (68 per cent). They found that 27 per cent of laboratory guinea pigs and 5 per cent of rabbits had antibodies. Laboratory rat and monkey sera were negative. Serum titers varied in dairy herds from completely negative in two herds to 48 per cent in another (all in the same locality). Groups of dogs, sheep, and swine showed variation of serum dye test antibodies. These and other studies indicate the wide prevalence of the disease.

The method of spread of this infection in individuals and species is incompletely understood.

It is known from animal epidemics[2] that large numbers may die and that Toxoplasma is found widely distributed throughout their tissues. In isolated cases Toxoplasma has been found in the urine of infected rabbits and dogs and in feces from dogs with a type of hemorrhagic colitis. It has been demonstrated in muscle tissue, heart, liver and spleen of many diseased animals.

Experiments prove that healthy mice can be infected by ingestion of other mice recently dead of an infection[34] and that infected mother mice can transmit the disease to the nursing offspring of healthy mothers.[4] Weinman and Chandler[39] transmitted the disease by feeding pigs and rats the tissues of other pigs, rats, and mice infected with a Toxoplasma strain isolated from pork. Van Thiel and van der Waaij[37] showed that consumption of tissue containing Toxoplasma pseudocysts leads to infection in mice and guinea pigs.

The site of entry of the organisms in causing *human* infections is not known. The foregoing studies suggest that oral transmission may be important. However, it is most likely that the disease is transmitted by various means. The results of investigations on transmission by arthropods and insects are inconclusive, and further study is indicated.

Clinical Manifestations

Human toxoplasmosis may appear in various forms, which often resemble other diseases and are not diagnosed as toxoplasmosis because they are not recognized as such.

The following modified classification of toxoplasmic infections as outlined by Frenkel[14] and Siim[36] is acceptable and will be discussed as listed.

I. Congenital
   A. Apparent
   B. Inapparent

II. Acquired
   A. Exanthematous
   B. Meningoencephalitic
   C. Lymphadenopathic
   D. Ocular

I. CONGENITAL TOXOPLASMOSIS

Early reports on congenital toxoplasmosis gave the findings in infants born with manifest infections, or who developed such infections within a short time after birth. Most infants had severe lesions of the central nervous system and the viscera. Mental retardation, hydrocephalus, and other sequelae were common.

It now is apparent that the disease also exists in a milder form and subsides without obvious sequelae.

Apparent Infections

The stage of pregnancy at which infection takes place, the virulence of the organism, and fetal or maternal resistance determine the type of infection in the newborn infant. The disease is transmitted to the fetus from a mother who acquired the infection during pregnancy, and the organisms most likely reach the fetus through the placenta.[10] The method of acquisition of the maternal infection is unknown, but all such infections occur without symptoms. Mothers who have given birth to toxoplasmic infants do not infect subsequent offspring. This suggests that maternal immunity is important in preventing acute toxoplasmosis in the fetus. It is not proved, however, that nonapparent infections do not occur in the fetus during subsequent pregnancies. Infection with organisms of low virulence also may result in milder infections, as illustrated in the subsequent report of one of our cases.

Infection early in pregnancy results in fetal death. Infections in midpregnancy cause widespread disease in the fetus, resulting either in death with miscarriage, or causing such severe damage

that the infant is born with marked sequelae of this disease (hydrocephalus, microphthalmus, etc.). Infections occurring late in pregnancy are associated with the acute manifestations of toxoplasmosis. Encephalomyelitis (generalized convulsions, fever, various paralyses), chorioretinitis, and visceral involvement may be observed. The infant may or may not survive. At other times the acute manifestations do not appear until a few days after birth. Eichenwald[5] found that 30 per cent of his patients with congenital toxoplasmosis were probably infected late in intrauterine life, because they were born with an acute generalized febrile disease and variously exhibited jaundice, anemia, diarrhea, vomiting, lethargy and irritability. Examination of these patients revealed an enlarged liver and spleen, petechiae, and purpuric or small erythematous papules with necrotic centers. An interesting observation was that six infants had a low grade fever and irritability, without other manifestations, and recovered completely without developing chorioretinitis; however, two of them later showed mental retardation.

Inapparent Infections

Some infants are born with the disease, which is unrecognized by the physician or parents. At a later date the child may exhibit serologic or clinical evidence of the infection. Some cases which have been reported as examples of acquired toxoplasmosis in children may, in fact, be examples of an activated phase of a congenitally acquired infection. In our experience this has been especially true with respect to ocular disease.

Chorioretinal Inflammations

A. Acute

1. Present at birth or shortly thereafter and associated with acute systemic disease
2. Developing after birth, and not always associated with acute systemic infection

B. Subacute

C. Late relapse of a healed chorioretinitis

Acute chorioretinitis, present at birth or shortly thereafter, is one of the most constant lesions to occur in congenital toxoplasmosis. It is most often bilateral and may occur in multiple foci. The disc and peripapillary region are commonly affected. Lesions occurring in this area most often lead to serious visual loss. The fundus lesions are usually found in those children with systemic manifestations of toxoplasmosis. In 1953 Feldman[8] studied 103 cases in which the diagnosis was based on the clinical and serologic findings. He found chorioretinitis in 99 per cent, and it was bilateral in 85 per cent.

Eichenwald[5] found 40 per cent of 75 toxoplasmic infants to have chorioretinitis at the first examination. The frequency increased to 80 per cent when the survivors were examined subsequently. He later presented the results obtained in a series of 140 patients, of which 80 per cent showed evidence of chorioretinitis.[6] Six of the 28 patients which did not show chorioretinitis at birth developed eye lesions within two weeks to six months after birth. Four of these six patients eventually showed bilateral involvement.

This later appearance of the chorioretinal lesions is fascinating and indicates a possible intermittent parasitemia. The infection in such patients may smoulder, with intermittent relapses, parasitemia, and involvement of other organs. Verlinde and Makstenieks[38] repeatedly isolated Toxoplasma from the cerebrospinal fluid and blood of four living infants having hydrocephalus, calcification of the brain, microphthalmia and chorioretinitis (one case as long as

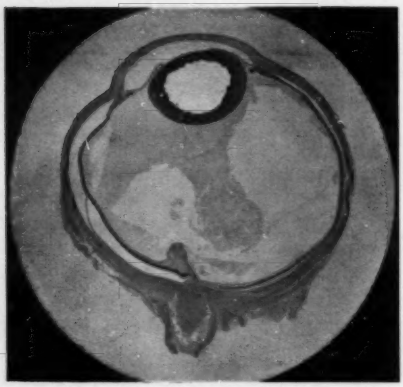

FIG. 1—Congenital toxoplasmosis, acute chorioretinitis.

two months after establishment of the diagnosis). Relapses of congenital ocular toxoplasmic infections, often with lesions in new areas of the fundus, suggest that infections may spread from rupture of pseudocysts and dissemination of organisms by the ocular fluids.

Pathology. The acute chorioretinal inflammation commences in the retina, with copious exudation into the vitreous, producing a marked haze (fig. 1). The foci are poorly defined and usually quite large (figs. 2 and 3). Secondary involvement of the choroid causes marked elevation (fig. 4). Small satellite foci are common. The acute phase of the inflammation lasts from two to four months, depending on its severity and the presence or absence of new foci. Organisms can be found in cysts or free in the acute lesions (fig. 5). After healing, the lesions are atrophic and pale with a variable amount of pigmentation at the margins (figs. 6 and 7). Pseudocysts may be found in the tissues adjacent to healed lesions. These are parasitized cells containing resting, viable organisms and are surrounded by a membrane which stains with silver. Rupture of these cysts may lead to reactivation of the disease.

Diagnosis. One cannot make a definitive diagnosis based on the clinical appearance of the eye lesions. It can be made with some certainty when combined with the associated systemic findings and by the serologic studies. The normal infant may have a low titer of dye test antibodies in his serum which persists up to four or five months after birth, as the result of passive transfer from the mother. The toxoplasmic infant is born with a high titer of antibodies if the infection developed early in the mother's pregnancy, or it develops increasing amounts of antibodies if the infection developed nearer term. The dye test antibodies develop within three to four weeks after onset of the disease and rapidly reach a high titer, whereas complement fixing antibodies do not develop until five to six weeks after onset of the infection. Both types of antibodies persist in fairly high titer for five to six years, then gradually decrease. Any dye test titer in a child below age 10 is of great significance, because surveys have shown that normal children below this age rarely show any antibodies against toxoplasmosis. A combination of acute disease of the eyes, the central nervous system and the viscera, with a high or rising dye test antibody titer, usually establishes the diagnosis. Animal inoculations of blood and spinal fluid from suspected cases should always be made, if possible, for a definitive diagnosis.

Subacute chorioretinitis may develop in a toxoplasmic infant who shows no signs of systemic disease, or who has had such mild signs that they are unrecognized. Such infants later may show evidence of damage to the central nervous system and may develop recurrent convulsions or other neurologic disorders. Examination of the eyes shows chorioretinal lesions which may be active or almost completely healed. The

FIG. 2—Congenital toxoplasmosis, acute chorioretinitis and papillitis.

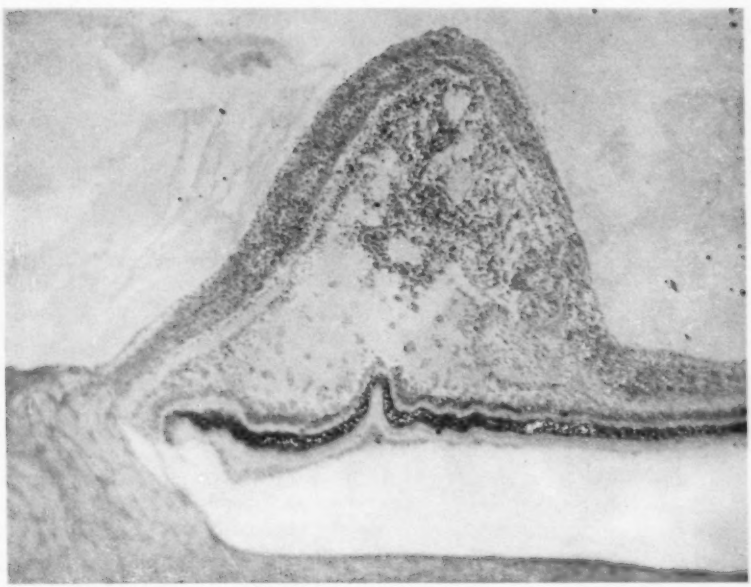

FIG. 3—Congenital toxoplasmosis, focal retinitis.

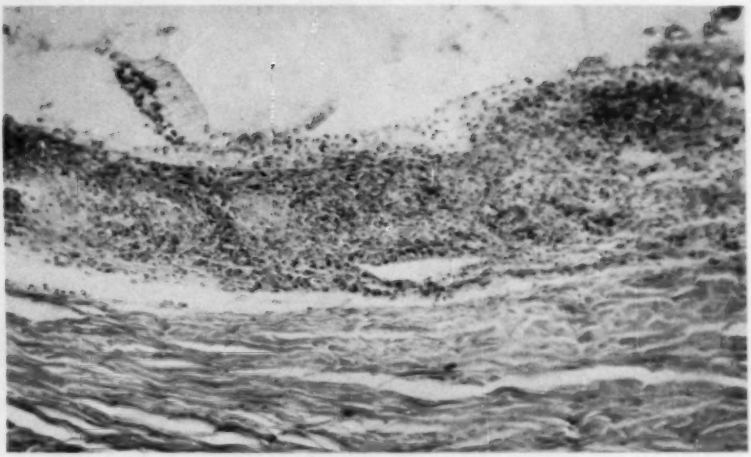

FIG. 4—Congenital toxoplasmosis, acute choroiditis with necrosis.

diagnosis in this group can be made with the same certainty as in the acute group.

Acute or subacute chorioretinitis in children beyond the stage of infancy becomes apparent to the ophthalmologist in a variety of ways:

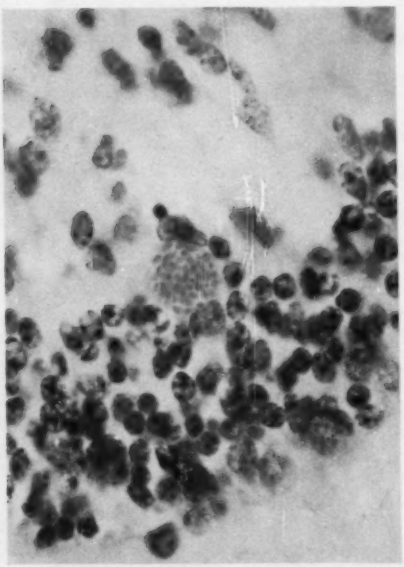

FIG. 5—Congenital toxoplasmosis, intracellular Toxoplasma in retina.

1. The child develops an esotropia or an exotropia. This results from macular or paramacular scarring, which can be observed easily on fundus examination. Roentgenograms of the skull may or may not show calcifications, and the blood usually reacts positively to dye and complement fixation tests. The child may show no evidence of cerebral damage or mental retardation, and he may be in perfect health otherwise.

2. The child is discovered to have reduced vision at the time he commences school, when the nurse checks the visual acuity. Examination shows changes in the fundi similar to those described previously, and general studies are substantially the same.

3. A *late relapse* of the chorioretinal inflammation occurs, causing progressive visual deterioration. Examination shows a chorioretinal scar with an adjacent new focus of chorioretinitis. This late relapse of congenital ocular toxoplasmosis has not been emphasized sufficiently. The

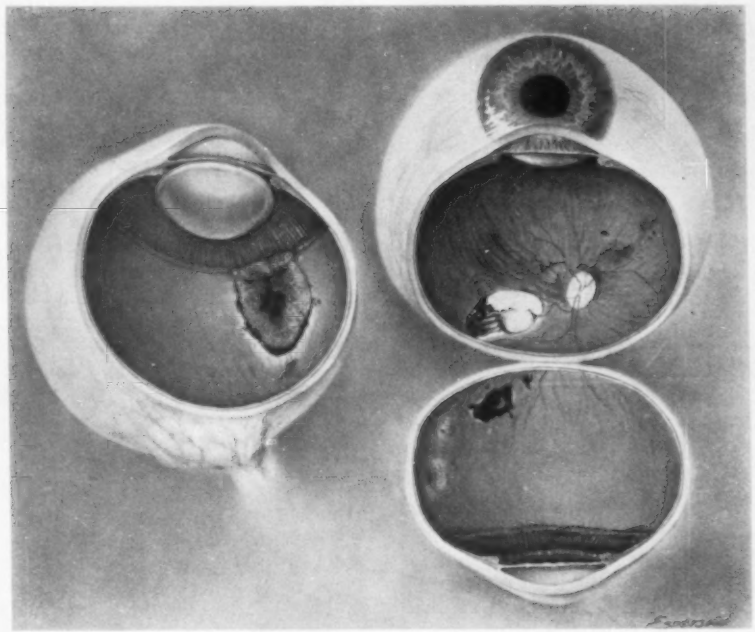

FIG. 6—Healed foci of chorioretinitis in congenital toxoplasmosis.

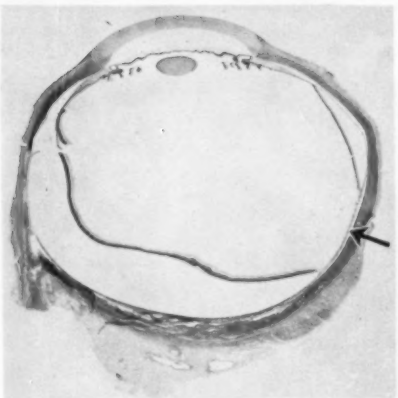

FIG. 7—Chorioretinal scar, congenital toxoplasmosis.

only previous references to this aspect of the disease are those of Woods and his colleagues[44] and of Eichenwald.[6] It should be repeated that many toxoplasmic infections are so mild that they are not recognized. In other infants the signs exhibited during a particular illness may not suggest the diagnosis of toxoplasmosis. The ophthalmologist and the pediatrician often are surprised to find an older child having clinical and serologic evidence of toxoplasmosis without a history of any previous acute illness.

Studies on Congenital Toxoplasmosis

In a routine survey of over 1,500 patients with various forms of endogenous uveitis, we encountered and have previously reported 28 patients with probable congenital toxoplasmic infections involving the eye.[17] Some of these were accompanied by evidence of systemic disease, while others were not. We have studied 8 additional cases, making a total of 36 (table II). In addition to these, we have

TABLE II
FINDINGS IN 36 CASES OF CONGENITAL TOXOPLASMOSIS

TYPE		ONSET			LATE RELAPSE	STRABISMUS	DYE TEST			SKIN TEST				SKULL X-RAY			
Uni-	Bi-	0-6 Mo.	6-12 Mo.	12 Mo.			<1:128	1:128-1:512	>1:512	+	—	+ —	Not Done	+	—	+ —	Not Done
11	25	8	9	19	12	20	14	13	9	22	9	1	4	7	21	7	1

found 4 interesting examples of a late exacerbation of congenital toxoplasmic chorioretinitis.

The mothers of all 36 children had normal pregnancies, and there was nothing in the history which would suggest a maternal toxoplasmic infection. Some had the usual contacts with household pets. An occasional mother had contact with domestic farm animals, but a history of illness of any of these animals was not obtained. Thirty-four of the infants seemed normal at birth except that one had feeding difficulties and another had signs suggesting cerebral palsy.

Strabismus (esotropia or exotropia) was the first and most common eye complaint, being present in 20 of the 36 children. It most often resulted from amblyopia due to macular inflammation or scarring. In 25 children the chorioretinal lesions were observed in both eyes, usually in the macula of one eye and at some other site in the other eye. Multiple foci were common. Only one patient showed a microphthalmia. The ocular disease became apparent to the parents of 8 patients before the sixth month after birth, and in 9 other patients it had a very early onset. Roentgenograms of the skull revealed no abnormality in 21 children, and showed positive signs of toxoplasmosis in 7 children. No roentgenograms were made in 7 cases, and in one case the interpretation of the roentgenogram was questionable.

Twenty-two patients had positive skin tests, nine were negative, one was questionable, four were not tested. *Nine patients had negative skin tests,* but did show positive dye tests, often in high titer. This would seem to demonstrate that the skin test alone cannot be used for the diagnosis of congenital toxoplasmosis.

Fifteen children 10 years of age or below had positive dye tests as follows: Six were 1:512 or greater; six were 1:128 to 1:512; three were below 1:128. The dye test titers in the 36 patients were as follows:

TITER	NUMBER OF PATIENTS
1:16	5
1:64	9
1:128	3
1:256	8
1:512	2
1:1,024	3
1:4,096	1
1:8,192	2
1:32,768	2
+ neutralization test	1
Total	36

It is interesting that 12 of these 36 patients had late childhood or adult relapses of chorioretinal inflammation. In some the fundi showed old chorioretinal scars with newer acute inflammatory areas in a "satellite" position.

Case Report: Late Relapse of Congenital Toxoplasmosis

Two of these cases have been report-

ed but will be recorded again in brief form to demonstrate the nature of this type of case.

Case 1.* M. F., age 12, a white male, was first seen because he had sudden diminution of vision in his good left eye. At the age of one and one-half years he was found to have a chorioretinal scar in the macula of the right eye. There were no further difficulties up to the age of 12. Examination showed the right vision to be 15/200 and the left to be 20/200. The right macula contained a large area of healed chorioretinitis (fig. 8). A heavy vitreous haze was evident in the left eye, and an indistinct massive yellowish area of inflammation extended from the disc to the temporal periphery (fig. 9). Roentgenograms of the skull showed calcifications (figs. 10 and 11).

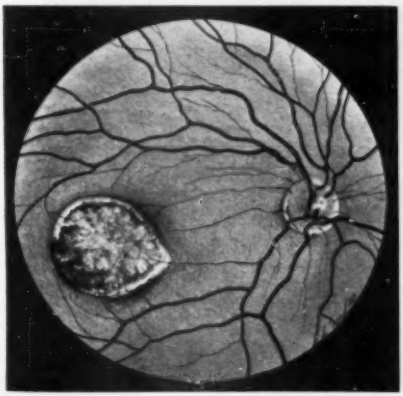

FIG. 8—Case 1, right eye, congenital toxoplasmosis.

FIG. 9—Case 1, left eye, congenital toxoplasmosis.

FIG. 10—Case 1, cerebral calcifications, congenital toxoplasmosis.

FIG. 11—Case 1, cerebral calcifications, congenital toxoplasmosis.

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FIG. 12—Case 1, chorioretinal scarring in congenital toxoplasmosis. Toxoplasma recovered from this eye on inoculation into mice.

TABLE III

HISTORY AND FINDINGS IN CASE OF CONGENITAL TOXOPLASMOSIS

CASE 1. PATIENT M. F.

AGE	1-½ YEARS	12 YEARS	20 YEARS
C-R	RE, Macular, Healed	LE, Acute, Temporal, Diffuse	LE, Secondary Glaucoma
Dye Test		1:128	
Skin Test		Positive	
Lab.		X Ray +	Toxoplasma Isolated from Enucleated LE

The methylene blue dye test was 1:128, and results of both the skin test and the neutralization test were positive.

Course: The course of the disease is shown in the accompanying table (table III). Five months after the onset of the disease the left vitreous had cleared so that vision was 20/70. Two and one-half years later the lesion was fairly well healed and vision was 20/100. There was extensive scarring and pigmentation of the entire temporal fundus, particularly along the horizontal meridian. Relapses occurred in this eye, and vision was eventually lost. The eye became divergent, hypotonic, and cataractous, and commenced to shrink. Enucleation was requested and accomplished in 1956. The eye was opened under sterile conditions and showed extensive scarring of the retina (fig. 12). The scarred area was used for cultures, only a small amount being saved for histologic study. Toxoplasma was isolated in mice from the healed lesions in this eye. The organism recovered has been found to possess a low viru-

lence for mice, requiring from eight to ten days to produce illness instead of the usual four required by the more virulent RH strain. When a small inoculum is made, the mice become ill but recover and live indefinitely, although most show some sequelae of the encephalitis. Inoculation results in significantly positive dye test titers in mice, and in previously negative rabbits and guinea pigs after inoculation by various routes.

Comment: This is a most interesting case in that it demonstrates a probable persistence of the organisms in the eye for twenty years following a typical congenital infection.

Case 2. M. W., age 11, a white male, was first seen at the age of 11 because of blurred vision in both eyes. Information was obtained that reduced vision had been discovered in the right eye at the age of 10. A general examination for a cause of this condition was negative. The patient was referred to me with the possibility that the eye lesions were of toxoplasmic origin. It was reported by letter that a methylene blue dye test in November 1954 at the Communicable Disease Center, Chamblee, Georgia, showed a titer of 1:64. There had been no systemic infection between the ages of 10 and 11 years.

At our first examination in December 1955 the eye lesions were completely quiet and fundus examination showed bilateral healed macular scars, more marked in the right eye (fig. 13). Vision in the right eye was 16/200 and in the left, 20/30. The methylene blue dye test titer was 1:4,096. Roentgenograms of the skull were negative, and the results of the skin test were negative. Results of an examination in May 1956 were essentially the same, and the dye test titer remained at 1:4,096.

A relapse of the inflammation in the left eye occurred in March 1957 without causing a change in dye test titer but causing reduction of vision to 20/80. The patient was treated with Daraprim and sulfadiazine and Meticorten by mouth, and the response seemed good. By May 1957 vision was improved to 20/50 and the lesion was healed. The dye test at this time was 1:256.

Comment: This type of early recurrence is the typical form observed in most of our cases of congenital toxoplasmosis. One might argue that this patient acquired his toxoplasmic infection at the age of 10, but we feel that it is of congenital origin because of our observance of undoubted congenital cases of identical type.

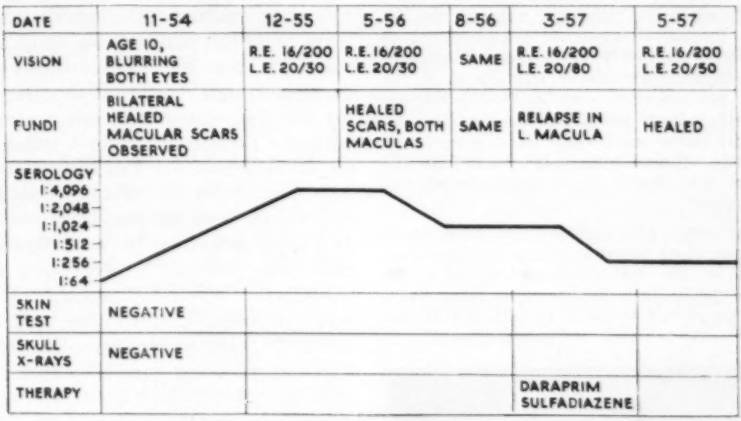

FIG. 13—Case 2, history and findings. Congenital toxoplasmosis with a late relapse.

Case 3.* A. L., age 36, a white female, was referred for examination because of blurred vision in her good right eye. She had a choroiditis in the left eye at age 15, and a recurrence at the age of 22. The last attack left markedly blurred vision in this eye (table IV).

Early in 1955, while on Okinawa, she de-

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TABLE IV
TOXOPLASMIC CHORIORETINITIS
PATIENT A.L., AGE 36, FEMALE

1936	1943	FEB.-MAY 1955
Acute Chorioretinitis, LE studies negative Cleared in 6 months after T & A	Acute Chorioretinitis, LE Central Vision Loss Pyrotherapy Cleared in 3 weeks leaving macular scar	Acute Serous Pleurisy diagnosed and treated as tubercular No Acid Fast Organisms demonstrated
← R.E. CLEAR →		

veloped pleurisy, dyspnea, headache, and fever. One week later a pleural effusion was discovered. The patient was returned to the United States and was treated with streptomycin and Isoniazid for six months for possible tuberculosis. In August 1956, six months after finishing the treatment, blurred vision developed in the right eye, although the patient thought it might have commenced in the latter part of 1955. A rather large area of peripheral choroiditis was found in the right eye and vision was 20/20. The left eye showed a large macular scar (fig. 14), although vision was 3/200. Skull plates were negative. The accompanying graph (fig. 15) shows the results of serologic studies and treatment.

Comment: This patient could have developed an acute pulmonic (acquired) toxoplasmosis in 1955, with subsequent spread to the right eye in 1956. We think it more likely that the chorioretinitis at ages 15 and 22 was due to congenital toxoplasmosis, and that the probable pulmonic relapse was due to rupture of a pseudocyst.

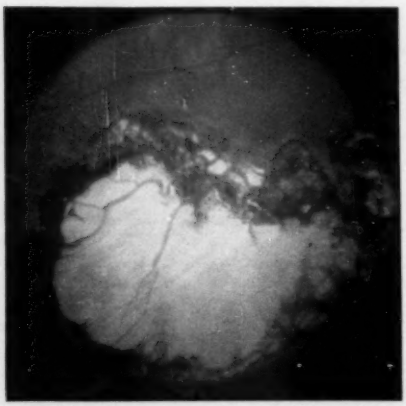

FIG. 14—Case 3, macular scar, left eye, due to chorioretinitis at ages 15 and 22 years.

We feel that some of the cases diagnosed as acquired toxoplasmosis are, in fact, late relapses of congenital infections. Several patients we have studied who have had such relapses have developed high dye test titers, suggesting that the relapse somehow reawakens antibody formation. Sabin[31] stated that his observations led him to believe that high amounts of toxoplasmosis antibody may result from subclinical reactivation of a latent infection. He described a patient who suffered a recurrence of a toxoplasmic infection, probably as the result of pseudocyst rupture, and were it not for some routine serologic studies which were being carried out, this relapse would not have been detected by those observing the patient.

Differential Diagnosis

The systemic manifestations of congenital toxoplasmosis must be differentiated from other infectious and degenerative diseases of the central nervous system. The ocular lesions are not diagnostic in themselves, but when coupled with the other signs they are suggestive. If the child shows *only* the ocular changes, one must depend on the results of serologic studies. One of the conditions to be differentiated was first reported by Sabin and Feldman[33] and dis-

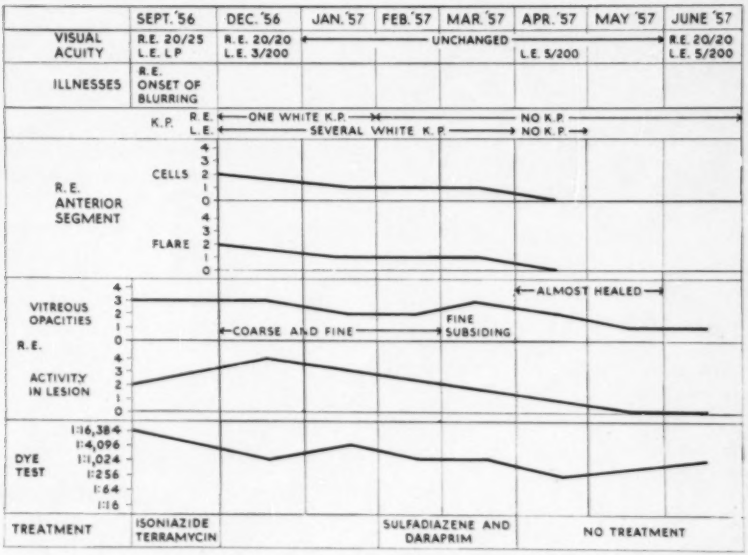

FIG. 15—Case 3, congenital toxoplasmosis.

cussed in detail before this society in 1949. In this syndrome the infants exhibit all the manifestations of congenital toxoplasmosis, yet they do not have positive serologic tests nor can Toxoplasma be isolated from the tissues. This disease has come to be known in pediatric circles as the Sabin-Feldman syndrome. The recent report of Weller and coworkers[40] of the isolation of an intranuclear inclusion producing virus from urine and liver aspirations of infants with illnesses resembling cytomegalic inclusion disease fits in with this entire picture. The latter infants had chorioretinal lesions and disease of the central nervous system similar to that reported by Sabin and Feldman. Christensen and his colleagues[1] also reported a case in which such lesions were observed in the brain, and at autopsy cytomegalic inclusion virus was demonstrated in the eye and brain tissues.

Other congenital inflammations of the eyes resulting from the spread of infection from the mother to the fetus must be differentiated from toxoplasmic disease. The absence of positive results on dye tests rules out toxoplasmosis.

II. ACQUIRED TOXOPLASMOSIS

A. Exanthematous

A number of cases of the exanthematous form of acquired toxoplasmosis have been reported. The disease resembles a rickettsial infection with a sudden onset, chills, fever, and development of a maculopapular eruption during the first week. The widespread involvement is suggested by the development of pleuritis, a dry cough, myocarditis, and encephalomyelitic symptoms. Most cases have been fatal. Eye involvement has not been recorded.

B. Meningoencephalitic

The meningoencephalitic form appears to be rare, the first case being reported by Sabin.[30] This 6-year-old boy

had a fever, became unconscious, had generalized convulsions, and developed lymphadenopathy. Examination showed a large number of mononuclear cells in his spinal fluid. At autopsy Toxoplasma was isolated from the brain, and there was a diffuse meningoencephalitis. Other cases have been reported by Siim (Denmark),[36] Feldman (United States),[9] and Giroud and co-workers (three cases from North Africa).[16] These patients had illnesses similar to that reported by Sabin. The patient whose case was reported by Feldman also had an exanthematous skin reaction. Eye involvement has not been observed.

C. Lymphadenopathic

The lymphadenopathic form will be reported in more detail because it may be the type which eventually causes eye lesions. Siim[35] in 1950 described such cases in a group of children. This investigator and others have emphasized the frequency with which this form occurs compared to other types. The three recognized forms are (1) a febrile lymphadenitis, (2) a nonfebrile lymphadenitis, and (3) a subclinical form.

Febrile lymphadenitis may have an acute or gradual onset with chills and fever, general malaise, headache, and localized or generalized lymphadenitis. It resembles infectious mononucleosis except for the negative results of the heterophile antibody test. The fever and lymphadenitis gradually subside over a period of three or four weeks. One case reported by Siim had retinal exudates and very fine hemorrhages in one eye. It is possible that this was due to febrile retinopathy. Results of the methylene blue dye and complement fixation tests become strongly positive late in the disease. Siim was able to isolate Toxoplasma from affected lymph nodes in a number of cases.

The *nonfebrile* form may be discovered by the patient or the parent. It may be evidenced by enlarged lymph nodes in an otherwise healthy patient.

The *subclinical* form apparently is uncommon. Siim reported the case of a healthy girl who was admitted to the hospital for study of an oligophrenia of nine years duration. A routine dye test showed a high titer, and examination then revealed some enlarged axillary and inguinal nodes. A node was excised, and Toxoplasma was isolated from it upon animal inoculation. According to Siim, results of clinical examination of these patients with lymphadenitis were normal except for enlarged nodes, which are of hazelnut to walnut size, relatively nontender, and generalized.

In the group of lymphadenopathy patients the disease runs a benign course, with complete recovery within a few weeks or months, but with the nodes often remaining enlarged for a year or longer. Lassitude was a common accompaniment of the convalescent period. It is interesting that only one of about 100 cases showed a chorioretinitis. The dye and complement fixation test became positive in one month, reaching dye test titers of 1:1,000 to 1:10,000 and complement fixation titers of 1:50 to 1:100. A relative lymphocytosis of 50 to 70 per cent was present in the blood.

According to Siim,[36] the histologic picture in the nodes is so characteristic that it should suggest the diagnosis and warrant serologic studies. Examination of sections of excised lymph nodes shows hyperplasia of the reticulum cells and islands of large eosinophilic cells scattered over the whole of the section.

To confirm the diagnosis, the surgically removed lymph nodes were minced, and the heavy tissue suspension was injected intraperitoneally into mice. An inapparent infection resulted, and at the time the mice were sacrificed six to eight weeks later the results of the sero-

logic dye tests were positive and Toxoplasma organisms were recovered from the tissues. Siim reported the isolation of Toxoplasma in this manner from the lymph nodes of 10 patients. Subsequently, Desmonts and Le Tan Vinh[3] isolated Toxoplasma from the nodes of 7 out of 19 subjects suspected of having acquired toxoplasmosis and exhibiting positive dye test titers. In 27 control patients it was not possible to isolate organisms from nodes.

D. Ocular

Early studies indicated that some cases of adult chorioretinitis were due to toxoplasmosis. It was soon learned that chorioretinal inflammations are rare in acute acquired systemic toxoplasmosis in contrast to their incidence in congenital toxoplasmosis. The reason for this is uncertain but it has been suggested that fetal retina is more susceptible to such infections. The occurrence of toxoplasmic chorioretinal inflammation in the *absence* of obvious systemic disease would seem to nullify this concept.

The ophthalmologic literature, however, contains a number of reports of ocular toxoplasmic infections, many of which are based on insufficient evidence. The probable diagnosis of ocular toxoplasmosis cannot be made solely on serologic evidence unless there is an unusually high titer, or at least a fourfold change in titer in paired sera. Even such changes as this must be regarded conservatively. One should beware of making positive statements based solely on the serologic findings.

A conclusive diagnosis of a toxoplasmic infection can be made only by isolation of Toxoplasma from the fluids or tissues of patients with acute illnesses. Such a requirement is impossible in those patients with ocular toxoplasmosis because these patients rarely have associated systemic infections and uncommonly show changes in serum dye test titers. Most often the ophthalmologist must be content with very presumptive laboratory and clinical evidence.

Frenkel[15] observed that those patients with positive results on skin tests had an earlier onset of chorioretinitis than those with negative results, and that the incidence of positive results of skin tests in patients with chorioretinitis far exceeded the incidence of positive results in a control group.

Wising[42] reported the first case of acquired ocular toxoplasmosis occurring during the course of a systemic disease. The infection occurred in the later stages of a febrile illness in a 31-year-old woman with a generalized lymphadenopathy. The serum of this patient showed a marked rise in dye test titer during the course of the illness, and the complement fixation test showed the characteristic delayed rise in titer. A number of other reports followed in which the presence of acute chorioretinitis was associated with a high or rising antibody titer.[18,24,27,28,44]

Following this, surveys on patients with chorioretinitis showed a higher incidence of positive results from dye and skin tests than in a similar group of the "normal" population, suggesting that a number of cases are toxoplasmic. The difficulty is that most patients with chorioretinitis who have positive results on tests also have very low titers. A number of investigators have tried to establish the significance of various dye test titer levels. Our group feels that any patient with chorioretinitis who has a positive titer at 1:16 or higher should be suspected of having ocular toxoplasmosis, provided that no other cause can be established. A single positive result does not prove that the patient has ocular toxoplasmosis; it serves only as a guide to indicate the possible presence of the disease.

The incident needed to stimulate further work was provided in 1952 by the studies of Wilder[21] in a report showing that organisms with the morphologic characteristics of Toxoplasma were present in the necrotic retina of chorioretinal lesions in 53 human eyes. These lesions were quite characteristic in that the principal focus seemed to lie in the retina, with secondary granulomatous reaction in the choroid and frequent thickening and inflammation of the overlying sclera. The disease was unilateral in most cases. The disease in most of these eyes had been considered on clinical or pathologic grounds to be ocular tuberculosis. Jacobs, Cook and Wilder[21] obtained 21 samples of sera from this group of patients at a later date. The following titers were found: one undiluted; one at 1:2; one at 1:4; seven at a titer of 1:16; four at 1:32; four at 1:64; two at 1:256; one at 1:2,048. There was some immediate objection to a morphologic diagnosis of ocular toxoplasmosis on these reported cases but, as one observer remarked, "What else could they be?"

In 1955 Jacobs and associates[23] analyzed the results of the skin test and the methylene blue dye test performed on 193 adult patients with uveitis. Eighty-six of these patients had a nongranulomatous form of the disease and 107 had a granulomatous type. The diagnostic criteria employed for the diagnosis of ocular toxoplasmosis in an individual case were as follows:

1. An ocular picture believed compatible with Toxoplasma infection
2. A positive toxoplasmin skin test, with the dye test positive to a minimum titer of 1:64
3. Exclusion of other systemic granulomatous infections

With these criteria, about 35 per cent of the 106 cases of granulomatous choroiditis were attributed to toxoplasmosis. This research team found an 80 per cent correlation between the skin test and the dye test in this group. In this and a former series, a total of 79 cases of ocular disease were found which could be considered to be toxoplasmosis. Fifty-one of the patients showed a focal choroiditis or chorioretinitis; 7 patients had old granulomatous chorioretinal foci with secondary acute allergic reactions superimposed; 17 had generalized uveitis; and 4 had retinal periphlebitis.

The final proof that Toxoplasma can cause chorioretinitis in adults was furnished by Jacobs, Fair and Bickerton[22] in 1954. They isolated Toxoplasma from the infected eye tissues of a patient who had suffered from a prolonged and relapsing type of chorioretinitis. Organisms also were observed histologically in the chorioretinal lesions.

RESULTS OF OUR UVEITIS STUDIES

We have conducted surveys on uveitis patients since 1947.* The following results have been obtained:

Methylene Blue Dye Test

There were 1,072 samples of sera on which methylene blue dye tests were done, and in which complete studies on the patients were available. The sera were grouped according to the type of disease present in the eye:

I. Iridocyclitis
II. Chorioretinitis
III. Panuveitis
IV. Miscellaneous (eye diseases other than uveitis)

Table V is a composite of data from

*I am indebted to Dr. Phillips Thygeson and Dr. Samuel Kimura for their advice and assistance in preparation of this paper. The three of us have collaborated for ten years in operation of the Uveitis Clinic at the University of California School of Medicine, and we have seen all patients included in the survey. We are also indebted to many ophthalmologists on the Pacific Coast, too numerous to mention here, for their cooperation in sending cases for survey, and furnishing information on the follow-up care.

TABLE V
DISTRIBUTION OF DYE TEST TITERS ACCORDING TO AGE OF PATIENT IN 1072 CASES OF UVEITIS (ALL TYPES)

DYE TEST TITERS	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85
1:4096	1		1					1				1						
1:1024	2					2	4	3	2	4	3	1	1					
1:256		2	1	3	3	6	9	4	8	7	5	1	3	3	1			
1:64	1	4	8	13	13	14	10	15	9	14	11	7	2	3			1	
1:16		1	6	10	18	19	27	20	12	18	9	12	7	4	2	1		
Neg.	3	19	20	23	62	82	88	86	85	77	55	41	24	22	7	3	2	

AGES BY YEARS

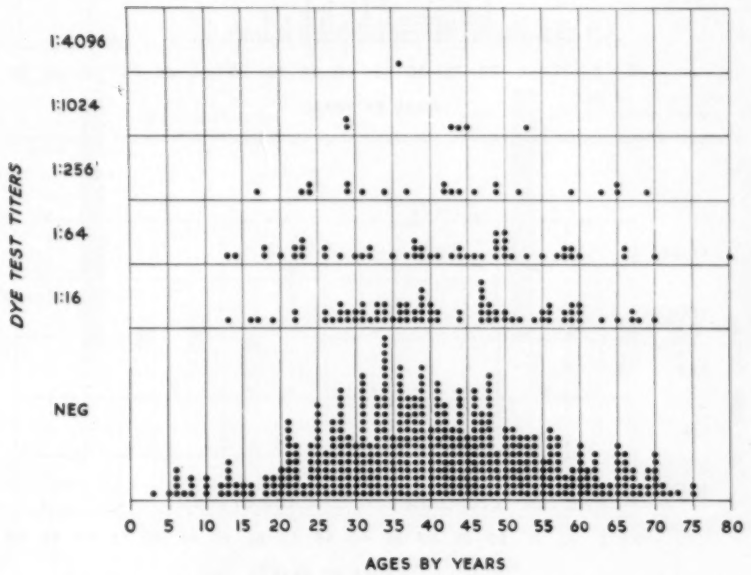

FIG. 16—Distribution of dye test titers according to age of patient in 649 cases of iridocyclitis.

groups I, II and III and shows the results of the methylene blue dye test in the various age groups. Forty-four per cent of sera were positive at a titer of 1:16 or higher.

The frequency of positive and negative tests in the various age groups can be estimated from the figures presented. It is known that the "normal" adult population in the geographic area represented by these tests shows about a 25 per cent incidence of tests positive in a titer of 1:16 or more. It is difficult to draw conclusions about the incidence of active ocular toxoplasmosis from these figures. The higher incidence of positive tests in the uveitis group suggests that toxoplasmosis plays an important part in the etiology.

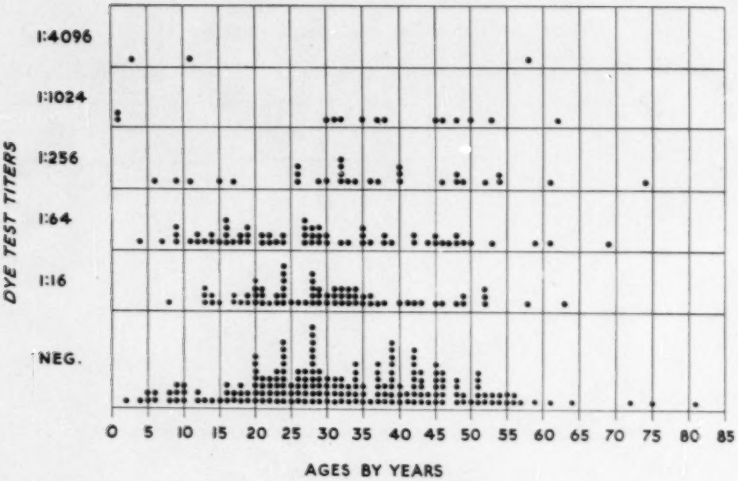

FIG. 17—Distribution of dye test titers according to age of patient in 375 cases of chorioretinitis.

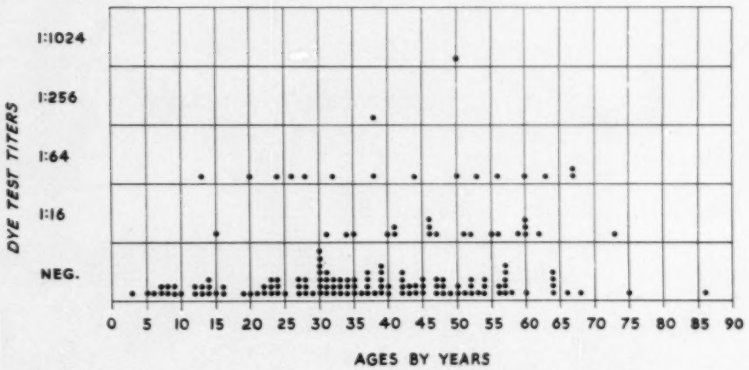

FIG. 18—Distribution of dye test titers according to age of patient in 158 miscellaneous cases.

The subgroups represented in this chart are shown in figures 16, 17, and 18, which show the titers in patients with iridocyclitis, chorioretinitis, and the miscellaneous (control) groups. The incidence of positive tests in the chorioretinitis group is 50 per cent, and the titers tend to be higher than in the iridocyclitis and miscellaneous groups.

Toxoplasmin Test and Methylene Blue Dye Test: Comparative Analysis

The correlation of the skin and dye tests in various types of uveitis and in the miscellaneous groups are shown in figures 19, 20, 21, 22 and 23. They confirm the results previously presented by our group. Of 617 patients with uveitis, 198 (32 per cent) had positive dye tests

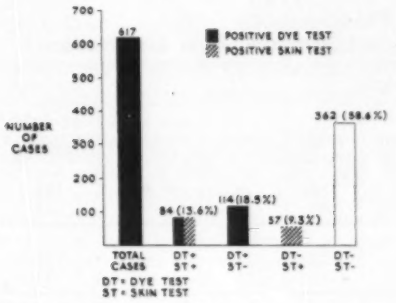

FIG. 19—Skin and methylene blue dye tests, all types of uveitis.

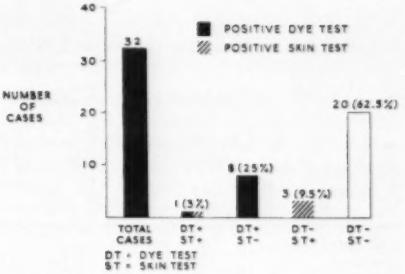

FIG. 22—Skin and methylene blue dye tests, diffuse uveitis.

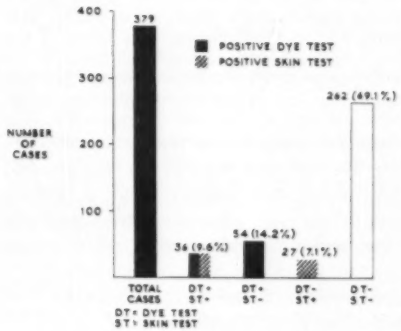

FIG. 20—Skin and methylene blue dye tests, iridocyclitis.

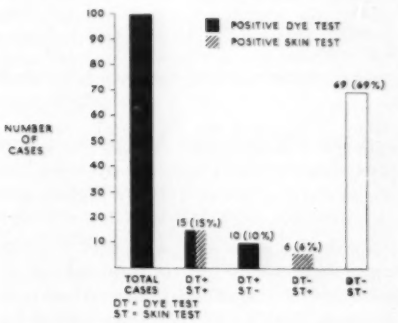

FIG. 23—Skin and methylene blue dye tests, miscellaneous.

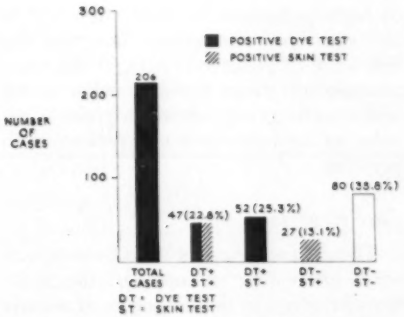

FIG. 21—Skin and methylene blue dye tests, chorioretinitis.

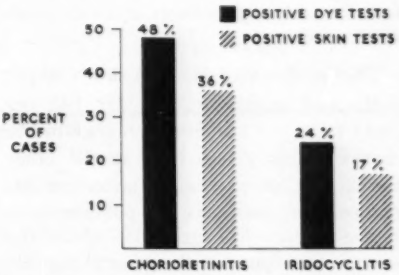

FIG. 24—Comparison of dye and skin tests: chorioretinitis (206 cases), iridocyclitis (379 cases).

TABLE VI

SKIN AND SEROLOGIC TESTS IN 1,241 CASES OF UVEITIS AND OTHER EYE DISEASES

	SKIN							SEROLOGY
	PPD	BRUC.	FREI	COCCID.	TOXO.	HISTO.	ALL SKIN TESTS NEG.	DT 1:16 OR HIGHER
C-R (386)								
Number	161	57	36	39	157	74	76	168
Per cent	41	15	9	10	40	19	19	43
I-C (670)								
Number	312	239	60	71	122	75	195	151
Per cent	46	35	8	10	18	11	29	23
Diffuse uveitis (57)								
Number	28	15	5	9	14	7	16	19
Per cent	49	26	8	15	24	12	28	35
Miscellaneous (128)								
Number	71	19	6	6	37	20	31	34
Per cent	55	14	4	4	28	15	24	26

and 141 (23 per cent) had positive skin tests. Eighteen and one-half per cent had positive dye tests at 1:16 or higher and negative skin tests. We have always considered the skin test as positive only when there are 10 mm. or more of induration at the end of 48 hours. Also, it is probable that some dye tests would be positive in a titer lower than 1:16. The correlation, therefore, might be closer if other criteria were accepted. Other observers have found this to be so. It is less easy to explain the group consisting of 9.3 per cent of the patients who had a positive skin test and a negative dye test. Possibly serum titers at lower levels were present.

The incidence of positive skin (36 per cent) and methylene blue dye (48 per cent) tests is considerably higher in the chorioretinitis group than in the other forms of uveitis and miscellaneous groups. The incidence of positive tests in the iridocyclitis group is about the same as that found in the general population. Figure 24 is a composite of the chorioretinitis and iridocyclitis groups to show the comparative frequency of positive dye and skin tests in the two groups. This study, too, suggests that a certain proportion of chorioretinitis patients have ocular toxoplasmosis.

Comparative Skin Test and Dye Test Findings

The preceding table (table VI) presents the results of all types of skin tests and the dye test in 1,241 uveitis cases. It is interesting that the frequency of positive results on the toxoplasmin test is as high as that on the tuberculin test in the chorioretinitis group, but that the incidence of positive results on the toxoplasmin test drops to 18 per cent in the iridocyclitis group, although positive results on the tuberculin test remain at 46 per cent.

Case Reports

The following cases have been selected as interesting examples of the problems involved in the diagnosis of uveitis and toxoplasmosis. Some have been chosen to illustrate the results of treatment.

Case 1. L. R., age 51, white male missionary.

We are indebted to Dr. C. P. Haseltine, Beaver Clinic, Redlands, California, for permission to present the findings in this unique case.

History: The patient was working in Peru in November 1953 when the symptoms of malaria appeared. He developed chills, headache, fever, and anorexia. This continued for a week, at the end of which time he first consulted a physician. He was placed in bed and given intravenous fluids. Blood smears for malaria were positive. He was treated with Camoquin Hydrochloride, which stopped the fever and chills. His convalescence was prolonged, and he had a disturbance of gait which persisted to the time when we first saw him (November 1954).

Two weeks after onset of the general illness, vision in the *right* eye became blurred and impeded by many floaters. At this time the patient developed a severe cough and was told that he had a virus pneumonia. The vision gradually became worse, and two weeks later the blurring occurred in the *left* eye. Following the pneumonia he was very weak and failed to recover properly from his illness. In May 1954 he was sent to Lima for ophthalmologic consultation. The diagnosis was bilateral chorioretinitis, and he was returned to the United States for treatment.

Prior to the onset of this illness the patient was exposed to insects (800 ft. altitude), but there were very few mosquitoes. He was working with a mule and some cattle, but they appeared to be healthy. The wife of another missionary had had several attacks of pneumonia while they were stationed at the mission.

At the first examination the vision in the right eye was 20/400 and in the left eye, 20/40. There was a moderate bilateral iridocyclitis. The right fundus showed a very large area of chorioretinitis superior to the disc, and a smaller one in the temporal periphery. The left fundus showed a large area of chorioretinitis superior to the disc, extending into the nasal and temporal portions of the fundus. Complete studies failed to reveal a cause for the illness or for the chorioretinitis. In November 1954, blood was sent to us for a dye test. The result was positive in a titer of 1:32,768. The complement fixation test was positive at a dilution of 1:64. A complete uveitis survey by our group in late November 1954 failed to reveal any other cause for the ocular disease. The right aqueous humor had a dye test titer of 1:16. By this time the general condition of the patient was excellent, and the general physical examination showed no abnormalities.

Course: Table VII and figure 25 show the clinical and laboratory findings on this patient and his treatment during the subsequent fifteen months. Treatment with Daraprim and sulfadiazine seemed to improve the ocular inflammation at first, and there was a temporary drop in the methylene blue dye test titer. Continued therapy failed to help, and there were exacerbations and remissions in the ocular inflammation. The patient was then given chloroquine, which seemed to result in improvement. Both the dye test titer and activity

TABLE VII

ACQUIRED TOXOPLASMIC CHORIORETINITIS

PATIENT L. R., AGE 51, WHITE MALE

DEC. 1953	JAN. 1954	FEB. 1954
Malaria, followed in 2 weeks by cough, and bilateral chorioretinitis.	Relapse malaria. Chorioretinitis still active.	Viral pneumonia. Chorioretinitis still active.

	OCT. 1954
Vision	RE—20/200 LE—20/40
Fundi	RE—3 + Coarse and Fine Vitreous Opacities. Chorioretinitis Superiorly and Temporally. LE—3 + Vitreous Opacities. Large Chorioretinitis Above Disc.
DYE TEST 1:32,768	

ACQUIRED TOXOPLASMIC CHORIORETINITIS
PATIENT L.R., AGE 51, WHITE, MALE

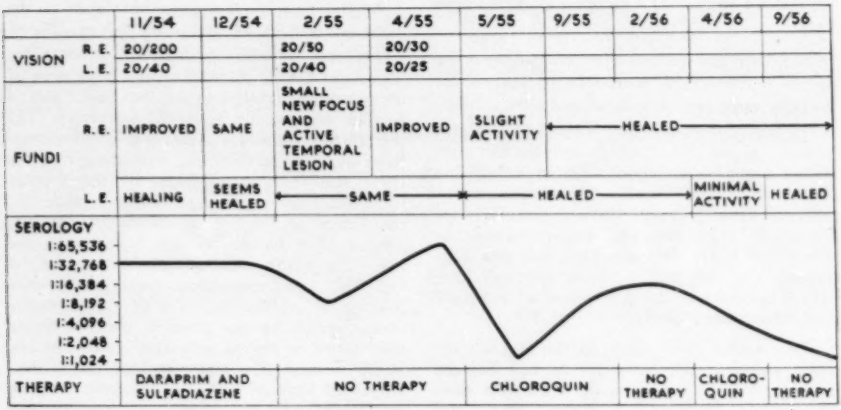

FIG. 25—Case 1, acquired toxoplasmosis.

of the lesions decreased. Eventually there was complete healing. By March 1956 vision in each eye was 20/20 and the patient returned to his missionary duties.

Comment: It is probable that the virus pneumonia which this patient had suffered subsequent to the malaria was really a toxoplasmic infection. It is interesting that the eye lesions came on at about the same time as the pulmonary infection. The persistence of high dye and complement fixation test titers in this patient for a year after onset of the pneumonia was of great value in the diagnosis. The low methylene blue dye test titer in the aqueous humor shows the lack of value of this test on aqueous humor. In view of the reported successful experimental and clinical studies on toxoplasmosis with Daraprim and sulfadiazine, it is difficult to explain the poor response of the eye disease to treatment.

Case 2. M. D., age 44, male army officer. We are indebted to Colonel Robert Kelley, Letterman Army Hospital, for permission to publish the findings on this interesting patient.

History: In July 1951, while in Cleveland, Ohio, this man developed a fever of 104° F., chills, and malaise, lasting about twenty-one days. He was treated at a Veterans Administration Hospital. The elevated temperature gradually returned to normal. At the time he was thought to have amebiasis, but no organisms were found. All other studies revealed no abnormality, including tests for brucellosis. He continued to have recurrent bouts of fever and chills following his transfer to the Army Hospital at Fort Sill. There were no pulmonary or skin lesions. About the first of November 1951 the patient observed that vision in the left eye was becoming cloudy, and a diagnosis of chorioretinitis was made. His visual acuity was 20/50 and there was a 6° scotoma (2/1000) just below fixation. He was treated with cortisone, streptomycin, penicillin, Aureomycin, and emetine and was discharged from the hospital in January 1952 much improved. The eye condition and fever recurred in March 1952 and again in September 1952. After this the vision was recorded as 6/200. While this man was in Austria in February 1953 there was a recurrence. In January 1957 he had a relapse and was seen at Letterman Army Hospital, San Francisco.

Examination: In January 1957, general physical examination showed no abnormalities. Vision in the right eye was 20/20 and in the left, 3/400. The right eye was normal. The left cornea showed some nonpigmented fine white keratic precipitates and there was a mild iridocyclitis. The left vitreous showed a moderate number of coarse and fine opacities. There were old healed flat chorioretinal scars in the extreme periphery at 4:00, 8:00, and 11:00 o'clock. The macular and perimacular areas showed scarring with some pigmentation covering an area of approxi-

mately one disc diameter. The patient was kept in the hospital for twenty days; the vitreous gradually cleared and the iridocyclitis disappeared.

A complete uveitis survey was repeated by us on June 11, 1957. A moderately positive reaction followed the first test dose of purified protein derivative (PPD), and strongly positive histoplasmin and toxoplasmin reactions were obtained.

Laboratory findings: The following positive methylene blue dye test titers were obtained:

2 /1/57 1:024
3/27/57 1:8,192 (almost positive at 1:16,384)
6/11/57 1:32,768

Course: In view of the quiescence of the ocular lesions, further treatment was not recommended. There have been no further recurrences of the eye symptoms or of the systemic condition (August 1957).

Comment: The close relation between the systemic illness and development of the ocular condition indicates that they were due to an identical etiologic agent. The failure to find a specific cause of the patient's illnesses in 1951 and 1952 suggests that he had had an active toxoplasmosis. The recurrences of his ocular disease also suggest such an infection. The diagnosis was confirmed by the high and rising titer in the serologic tests.

Case 3. F. G., age 53, white housewife.

We are indebted to Dr. Ulrich Fritschi of Sacramento, California, for permission to study and publish the results of investigations on this patient.

Chief complaint: Blurred vision, right eye, ten months.

History: The right eye became inflamed and the vision blurred in April 1955. There was very little pain. Examination showed large mutton-fat keratic precipitates, posterior synechias, many cells, and a dense flare in the anterior chamber. The pupil was dilated with difficulty and the fundus could be seen very poorly. Detailed laboratory and physical studies failed to reveal a cause for the uveitis. Within a few months after onset of the uveitis, the patient developed a rapidly progressive cataract. Because of failure of the disease to respond to streptomycin, Promizole, and hydrocortisone, the patient was referred to us for further evaluation.

Past history: The patient had poor vision and an exotropia of the left eye for many years. This eye had never been inflamed.

Examination: The right eye had fair light perception but poor projection. The intraocular pressure was normal, the cornea was clear, and there were old crenating mutton-fat keratic precipitates. The aqueous showed 2 plus flare and cells. The iris stroma was atrophic, and there were scattered posterior synechias. The lens was completely cataractous. The left eye had 20/70 vision and a high refractive error, and there was an inferior conus of the optic disc.

General physical examination and detailed laboratory studies failed to reveal a cause for the uveitis other than a probable toxoplasmosis.

Laboratory studies: Results of all skin tests were negative except that for toxoplasmin, which was strongly positive. The methylene blue dye test on the serum was positive in a titer of 1:1,024 and the aqueous humor titer was 1:128, which is unusually high. Subsequently the complement fixation test changed from negative to positive at a 1:10 dilution. Cultures of aqueous humor in tissue culture, fertile eggs, and on HeLa cells were negative.

Course: The patient was given a course of Daraprim and sulfadiazine by mouth, and the inflammation eventually cleared. We could not say whether a definite therapeutic response was obtained. A cataract extraction was done on the right eye in the latter part of 1956, and the patient was referred for further studies in March 1957. The results of the cataract extraction were excellent, but the upper fundus of the right eye showed a tremendous area of healed chorioretinitis, extending from the disc to the periphery and resulting in preretinal veiling and obscuration of the macular area.

Comment: The severity of the lesion in the fundus, granulomatous nature of the anterior ocular inflammation, rapidly progressive cataract, absence of other possible causes of the disease, and significantly positive serologic and aqueous humor studies point to this case as being one of ocular toxoplasmosis.

Case 4. F. H., age 32, white waitress.

Chief complaint: Blurred vision, one month.

History: Blurred vision developed in the left eye about the middle of September 1955. This was associated with pain in the eye and periorbital region. The patient was sent by her physician to an ophthalmologist who prescribed atropine, cortisone drops, and tetracycline by mouth. These failed to cause improvement, and she was referred for further studies.

Past history: Early in 1955 the patient had

been treated for a rather severe spastic colitis. No other disease could be related to the present episode. Her mother had developed tuberculosis when the patient was five years old, but results of follow-up tests in this patient were always normal.

Examination: During October 1955, the patient's vision was 20/20 in the right eye, and there was no evidence of disease. The visual acuity in the left eye was 20/100. There were 1 plus congestion, 3 plus flare, and 1 plus clot in the anterior chamber. There were no keratic precipitates. Fundus examination showed 4 plus vitreous opacities and a very large area of chorioretinitis in the lower nasal portion.

Laboratory studies: The reaction to the second test dose of PPD was positive, and the toxoplasmin skin test was markedly positive. The methylene blue dye test was positive in a titer of 1:64, and the complement fixation test was positive at 1:10. The sedimentation rate was elevated to 30 mm., corrected (Wintrobe). General physical examination revealed no abnormalities.

Course: Further dye tests during 1955 and 1956 showed the methylene blue dye test titer to range between 1:64 and 1:256. In April 1956, the titer rose to 1:1,024. During 1957 the titer remained fairly constant at 1:256 and results of the complement fixation tests were negative.

The patient was treated with chloroquine during November and December 1955, without effect on the ocular inflammation. Gradual clearing occurred by mid-January 1956, but about this time a new lesion appeared just above the old one. This new focus gradually cleared, and in February 1956 the patient had vision of 20/30 in the affected eye, and only 1 plus flare and cells in the aqueous humor.

The disease finally became quiescent and remained so until March 1957, when a severe acute relapse occurred. The visual acuity in the left eye was reduced to hand movements, and 3 plus cells and flare were seen in the aqueous humor. There were small white keratic precipitates. The patient was given Daraprim 75 mg. a day, sulfadiazine 2 gm. a day, and Meticorten 15 mg. a day. Fairly rapid improvement occurred, so that one month later the visual acuity was 20/70 and there was a plus-minus flare and cells in the anterior chamber. The vitreous continued to show about 3 plus cells and there was questionable activity in the chorioretinal lesion.

Comment: This case illustrates the difficulties involved in the diagnosis of possible toxoplasmosis. The low initial dye test titer in this patient's blood might have made the diagnosis of ocular toxoplasmosis questionable. However, the increasing titer, development of a positive complement fixation test and rapid response to Daraprim and sulfadiazine present strong evidence in favor of a toxoplasmic origin.

Case 5. M. S., age 48, housewife.

We are indebted to Dr. Dohrmann Pischel for permission to present the findings in this case.

History: In May 1951 the patient developed discomfort in the left eye, followed by congestion, blurring, and photophobia. This was treated, and over a period of six weeks it gradually cleared, but there was some residual blurring. In October 1951 there was a recurrence, persisting to March 1952, when we first saw the patient. Examination at that time showed that the right eye was entirely normal and that the left eye had 20/50 vision with 1 plus congestion, 3 plus cells and flare in the anterior chamber, 2 plus fine anterior vitreous opacities, and a rather large, very indistinct area of yellowish chorioretinitis along the superior temporal vessels. The patient was treated with cortisone, diathermy, Omnadin, and atropine, and the lesion gradually cleared.

In October 1952 there was a relapse. At this time a survey showed only a positive tuberculin test result in the first test dose of PPD. Results of toxoplasmin skin test and the methylene blue dye test were negative. The erythrocyte sedimentation rate (corrected) was 25 mm. (Wintrobe), and the white blood count was 10,400 per cubic millimeter. An explanation for the elevated sedimentation rate was not found. It was recommended that a biopsy of a neck gland be obtained (not done), and that the patient be treated with streptomycin and para-aminosalicylic acid. This was done and the disease gradually quieted, but the patient was left with very blurred vision. Subsequent exacerbations and remissions occurred.

We saw the patient again in February 1957 because of continued relapses. She was hospitalized, and a complete survey was repeated. The skin tests still showed a positive tuberculin reaction and a positive reaction to brucellergin. The toxoplasmin skin test was negative. The sedimentation rate was normal. Physical examination and other laboratory studies failed to show any abnormality except the methylene blue dye test titer, which was now 1:256 and arose to 1:1,024 a month later. During the next five months the dye test titers were 1:256. The complement fixation test remained negative.

In August 1957 the right eye was normal. The left eye had only light perception, and the cornea was quite hazy because of epithelial edema and a massive deposition of large mutton-fat keratic precipitates on the lower two thirds of the cornea (fig. 26). There were 4 plus cells and flare in the anterior chamber, extensive posterior synechias, a number of nodules in the iris stroma, and cataractous changes in the lens. The vitreous and fundus could not be seen, although light projection was fairly good.

Past history: In 1929 the patient had developed persistent diplopia. In 1934 she had had a left optic neuritis for two months with complete clearing. A recurrence of the neuritis occurred in 1948, and the vision was decreased for six weeks. She was told that it was possible that she had multiple sclerosis, but further symptoms of this disease have failed to develop. Other than several psoriatic lesions on her legs, she had always been healthy.

Course: The accompanying graph (fig. 27) shows the course of the disease and the treatment instituted for this patient. The response to Daraprim and sulfadiazine and Meticorten was excellent, and at the present time only very low grade activity can be seen in the anterior segment.

Comment: The reversal of a previously negative dye test to one which was positive is evidence of a toxoplasmic infection. The failure to respond to antituberculous drugs, and the fairly prompt response to sulfadiazine and Daraprim would tend to confirm our opinion that this is an example of ocular toxoplasmosis.

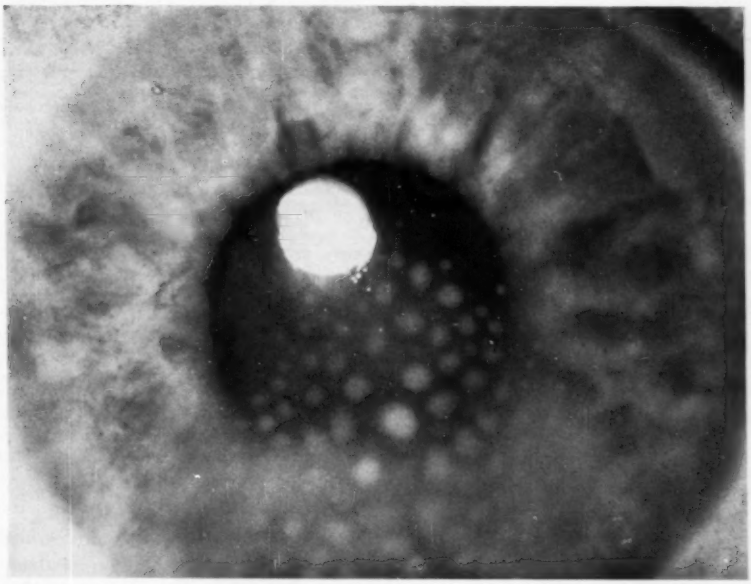

FIG. 26—Acquired ocular toxoplasmosis, severe anterior inflammation with mutton-fat keratic precipitates.

Therapy of Toxoplasmosis

Early studies showed an *in vitro* and *in vivo* sensitivity of Toxoplasma to sulfonamides and to some antimalarials. Subsequent clinical studies in humans with these drugs and chemicals were disappointing. Eyles and Coleman[7] later showed that Toxoplasma infections in experimental animals were responsive to combinations of sulfadiazine and pyrimethamine (Daraprim), an antimalarial, and that these combinations were syner-

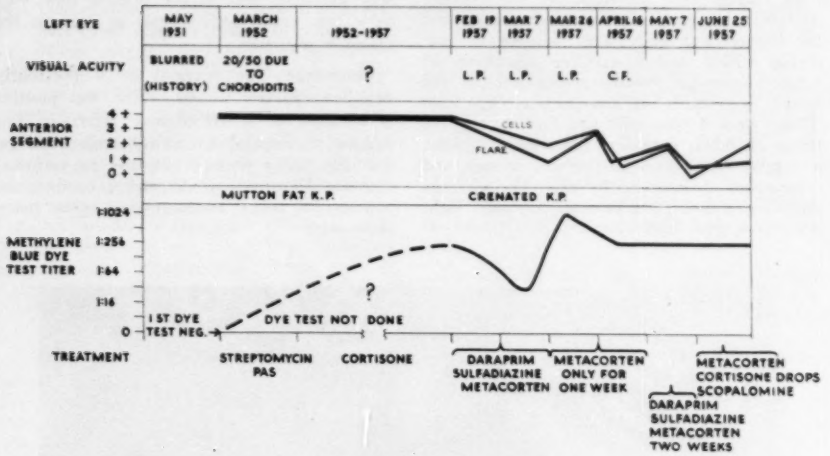

FIG. 27—Case 5, acquired toxoplasmosis.

gistic in their action. Ryan and co-workers[29] showed that these drugs were effective in human ocular toxoplasmosis. This was confirmed by Perkins and coworkers.[26]

Since the reports of Eyles, we have employed these chemicals, individually and in combination, in a fairly large series of patients. A number were given these medications in appropriate doses for two to three weeks. The treatment was usually carried out for a five day period, with a two day rest, followed by another five day course. Blood and urine studies were made at weekly intervals to detect drug toxicity. Occasional patients seemed to show a response, but the results have been disappointing. An improved outcome seems to have been obtained recently by the addition of prednisone or prednisolone to the above regimen. It is impossible to assess the results of such therapy in a large number of these patients because of the frequent uncertainty concerning the original diagnosis.

In 6 patients with almost certain evidence of a toxoplasmic ocular inflammation, only one showed a response to therapy which could be considered due to the treatment. In 12 other patients, some with evidence of a late relapse of a congenital infection or with probable acquired ocular disease, only 3 gave prompt response to this therapy. It should be noted that one fairly definite case (case 1) of acquired ocular toxoplasmosis reported in this paper failed to respond. It is not surprising that such chronic or long-standing cases should fail to respond to the medication, because the inflammatory exudate and reaction to the inflammation might prevent access of the drug to the organisms. These therapeutic studies can be summed up by saying that the outcome often was disappointing.

Summary and Conclusions

1. The acute manifestations of congenital toxoplasmosis are well established and include chorioretinitis, encephalomyelitis and visceral inflammation.

2. Ocular toxoplasmosis may be overlooked in an apparently healthy child until attention is directed to the eyes by

the development of a strabismus, by detection of amblyopia in one or both eyes during a routine eye examination, or by the development of increased blurring due to a late relapse of the chorioretinal inflammation.

3. Thirty-six cases of congenital ocular toxoplasmosis are reported. This study reveals that less than 20 per cent showed evidence of cerebral calcification which could be considered to be toxoplasmic; that the condition was unilateral in 30 per cent of the patients; that 33 per cent of the patients had a late relapse of the congenital infection; and that 55 per cent had a strabismus.

4. Nine of these patients had positive results of dye tests and negative results on skin tests, indicating that the skin test is less reliable for diagnosis than the dye test. Twenty-five per cent had dye test titers in excess of 1:512, and almost 30 per cent had titers between 1:128 and 1:512.

5. In addition to the 36 cases of congenital toxoplasmosis, we have observed four others with a late relapse of congenital toxoplasmic infections. Toxoplasma was isolated from the enucleated eye of one of these patients twenty years after birth.

6. Ocular inflammation rarely occurs during the course of acute postnatally acquired systemic toxoplasmosis, although some cases have been reported.

7. In uveitis cases, questionable enlarged lymph nodes should be excised for microscopic and cultural studies.

8. The methylene blue dye tests on 1,072 patients with uveitis in various age groups showed 44 per cent of the sera to be positive in a titer of 1:16 or higher. This can be compared to a 25 per cent incidence in a miscellaneous group of nonuveitis cases.

9. The correlation of results of the methylene blue dye test and the toxoplasmin test in 617 cases of uveitis revealed that in 32 per cent results of dye tests were positive and in 23 per cent results of skin tests were positive. Forty-eight per cent of patients with chorioretinitis reacted positively to dye tests and 36 per cent reacted positively to skin tests. This can be compared with 25 per cent and 18 per cent of the normal population in this area.

10. The various skin tests in 1,241 cases of uveitis and in a miscellaneous group disclosed that approximately 40 per cent of the patients with chorioretinitis and 18 per cent of the patients with iridocyclitis had positive reactions to toxoplasmin tests. In this same group, 43 per cent of those with chorioretinitis and 23 per cent of those with iridocyclitis had positive dye test titers. The percentage of incidence of positive dye and skin tests in the iridocyclitis group was the same as in the control group.

11. In the cases studied there were five of acquired adult ocular toxoplasmosis. Two of these were associated with acute systemic infections.

12. Daraprim and sulfadiazine therapy of acquired ocular toxoplasmosis was found to be disappointing, but further studies seem to be warranted.

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REQUISITES FOR POSTOPERATIVE THIRD DEGREE FUSION

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THE standard of perfection in surgical operation for strabismus is the attainment of single binocular vision with good stereopsis. But how does one achieve this result? Why does one patient develop a functional result and another fail to do so when the age of the patient, the deviation, the refractive error and the amount of correction done are essentially the same in each?

If one could tell from the clinical data which patients had a good prognosis for a functional result and which did not, then a high percentage of such results could be achieved in the favorable cases and much needless effort avoided in the rest. The purpose of this article is to point out which factors promote and which hinder the attainment of this ideal in surgical procedures to correct strabismus.

MATERIAL FOR STUDY

This survey, based on 256 consecutive surgical patients from private practice, consists of 96 patients with simple esotropia without hypertropia, 36 with esotropia and overaction of one inferior oblique, 67 patients with esotropia with overaction of both inferior obliques, 17 patients with simple exotropia without hypertropia, and 40 patients with various types of hypertropia with little or no horizontal squint, some of whom had congenital paralytic strabismus with fusion in some part of the binocular field of fixation. Of the entire group, 55.9 per cent had strabismus associated with hypertropia and 16.8 per cent had intermittent strabismus (table I).

Patients with purely accommodative squint or with cataract, aphakia, central choroiditis, optic atrophy, opaque media, or Duane's retraction syndrome, as well as patients whose history includes a previous operation or an acquired extraocular muscle paralysis, were excluded.

The parents were carefully questioned as to the child's age at the onset of squint and the initial nature of the deviation (constant or intermittent). During each visit the vision was tested with and without glasses, using the "E" chart when necessary. An atropine cycloplegic refraction was always done on the eyes of children, and full or almost full correction was ordered when indicated. The amount of strabismus was measured several times before operation with prisms and the cover test at 20 feet and at 13 inches with and without glasses, with the eyes in the primary position. The horizontal and vertical components of the deviation were also measured in eyes directed to the right and to the left at a distance of 13 inches, as well as in eyes straight up and in eyes straight down in the midline plane. When the cooperation was good, the vertical and the horizontal deviations were determined in the corners as well.

For patients under 6 years old with unilateral constant strabismus, continuous monocular occlusion was prescribed for a period of one to 36 months (average 14.5 months) to improve the vision of the amblyopic eye. Alternate occlusion was carried out in patients with

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TABLE I

TYPE OF STRABISMUS IN 256 PATIENTS WITH CONSTANT AND INTERMITTENT SQUINT

TYPE OF SQUINT	CONSTANT SQUINT		INTERMITTENT SQUINT		TOTAL NO. OF CASES
	NO. OF CASES	PER CENT WITH 3° FUSION	NO. OF CASES	PER CENT WITH 3° FUSION	
ST without HT	90	18.8	6	50.0	96
ST with IO_1	31	19.3	5	60.0	36
ST with IO_2	61	13.1	6	66.6	67
XT without HT	6	0.0	11	81.8	17
Assorted HT	25	4.0	15	60.0	40
Total	213	15.0	43	65.1	256

alternating constant strabismus to prevent active suppression and anomalous retinal correspondence. Active, formal orthoptic treatment was rarely given for amblyopia or suppression.

Each patient was examined an average of five times over an average period of 13.6 months before operation while waiting for the squint to become stabilized or for the amblyopia to improve. In preschool children an attempt was always made to correct the strabismus before school age. The amount of correction attempted in each instance was gauged to the amount of deviation present and usually divided between the two eyes except in the monocular cases. When one or both inferior oblique muscles produced 8 or more prism diopters of hypertropia in adduction, one or both inferior oblique muscles were usually myectomized or recessed. If the hypertropia measured less than 8 prism diopters in adduction, or was not constant in character, it was usually ignored and only the horizontal deviation corrected. In a few instances of isolated overaction of one or both inferior or superior oblique muscles, only the offending oblique muscle was subjected to surgical operation.

After operation the vision was recorded and the amount of strabismus measured with prisms and the cover test, as before operation. Tests for fusion were made at this time, using first the Worth four dot test for distance and near. The arrow test (fig. 1) in the stereoscope was used next to test for paramacular third degree fusion, after which macular stereopsis was elicited and graded by means of the Keystone DB card 6-33781 (fig. 2). Occasionally the fly test with polaroid glasses, the Verhoeff stereoscopic test, or some other stereoscopic cards were employed.

The stereoscope, rather than the synoptophore, was used to test for stereopsis because I believe that it approximates normal everyday third degree fusion more closely and gives fewer false positive findings than does the major amblyoscope. Also, the stereoscope, being simpler and quicker to use, enabled the examining physician to make these tests himself during a routine examination.

In no case was third degree fusion assumed to be present from the appearance of the eyes or their reaction to the cover-uncover test; patients with apparent binocular fixation were not classified as having a functional result unless they also passed these tests for stereoscopic vision. Several who were able to fuse the four dot test for distance and near failed all

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FIG. 1—"Arrow test" for paramacular fusion. When this card is placed in a stereoscope, a patient with paramacular stereopsis sees a 2-arrow weather vane, in which the top arrow points in one direction and the bottom arrow points at an angle of 90 degrees to the first. When suppression exists, one arrow always looks longer.

tests for third degree fusion, and a few who fused the arrow test failed the Keystone DB card test and vice versa. Thus, of the 60 patients who manifested stereopsis on these tests, 16.7 per cent had fusion on the arrow test only, 73.3 per cent had 20/200 to 20/15 macular fusion on the DB card test, and 10 per cent had third degree fusion on other tests.

As a rule none of these tests for stereopsis was entirely satisfactory for patients less than 5 years old. For this reason the younger children were re-examined when old enough to understand what was expected of them.

When last seen, the youngest of the 60 patients with postoperative third degree fusion was 5.5 years, the oldest was 52, and the average age was 13.75 years; the shortest follow-up was 6 months (two patients), the longest 19.5 years

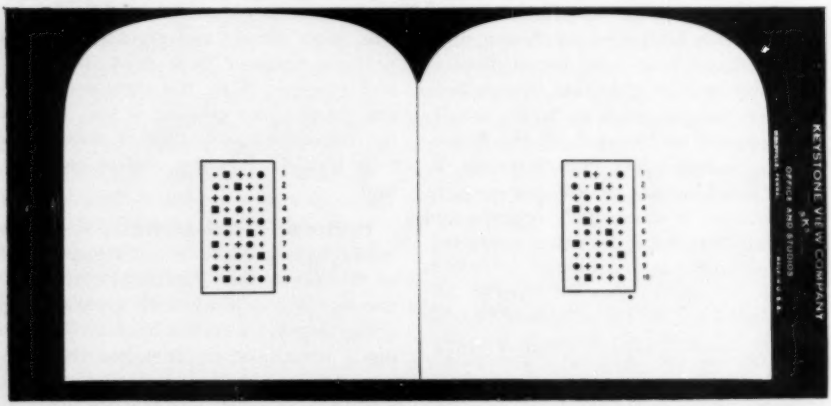
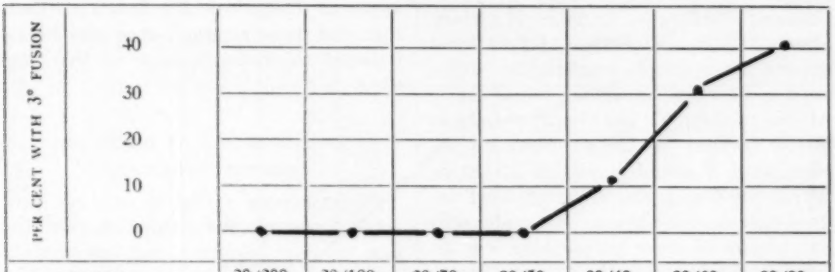


FIG. 2—Keystone test for macular fusion. When this card is placed in a stereoscope, a patient with macular stereopsis sees one of the five characters on each line "closer" to him than the rest. The degree of stereoscopic vision is graded from 20/200 in line 1 to 20/15 in line 10.

TABLE II

EFFECT OF VISUAL ACUITY ON THIRD DEGREE FUSION IN 256 CASES OF CONSTANT AND INTERMITTENT SQUINT



VISION	20/200	20/100	20/70	20/50	20/40	20/30	20/20
No. of Cases	37	10	16	17	18	70	88
No. with 3°	0	0	0	0	2	22	36
Per Cent with 3°	0	0	0	0	11.1	31.4	40.9

(one patient), and the average 5.3 years. Of the 60 cases, 93.3 per cent were followed for one year or more. When third degree fusion was absent, the average follow-up was somewhat less, being 3.8 years for 80 patients with amblyopia in one eye and 4.7 years for the remaining 116 patients with good vision in each eye.

In 59 of the 256 patients (23.3 per cent) a second operation accounted for the short follow-up. However, since the results of the secondary operations have been omitted in this analysis, all patients who required a second operation were classified, in this paper, as functional failures even though they developed stereopsis after the second operation.

ANALYSIS OF MATERIAL

The pertinent preoperative, operative and postoperative data for each patient were tabulated and correlated with the final result to learn which elements of the deviation favored and which prevented a functional result.

Factors of little or equivocal importance were the refractive error (except anisometropia of sufficient magnitude to cause amblyopia ex anopsia); the amount of esotropia, exotropia or hypertropia present before operation; the age of the patient at the time of operation; the type of operation done; the number of orthoptic exercises given; the presence or absence of anomalous retinal correspondence (testing was not always done before or after operation); obvious anatomical anomalies in the orbit or postoperative adhesions; manifest lesions of the optomotor pathways; heredity; and the position of the eyes under general anesthesia. These factors were considered to be of minor or of uncertain significance because no one of them alone seemed to play a dominant role in preventing or achieving postoperative third degree fusion.

In the text and the tables which follow, "full correction" indicates a residual horizontal deviation (phoria or tropia) of 10 prism diopters or less and a vertical of 2 prism diopters or less in the primary position, with glasses if needed. "Good vision" means 20/40 vision or better with or without glasses.

EFFECT OF VISUAL ACUITY ON THIRD DEGREE FUSION

The malignant effect of amblyopia ex anopsia on postoperative third degree fusion is illustrated in table II, which shows that the percentage of functional results increased dramatically from zero to 40.9 per cent as the visual acuity of the amblyopic eye improved from 20/50 (or less) to 20/20. Since no patient with a visual acuity of 20/50 or worse developed postoperative third degree fusion, it is obvious that amblyopia ex anopsia of these proportions was an insurmountable obstacle to achieving a functional result in surgically corrected squint.

When third degree fusion occurred in the presence of mild amblyopia, the quality of the stereopsis was always inferior, because no patient with 20/40 vision in the amblyopic eye developed better than 20/40 macular stereopsis. This observation on the limiting effect of poor vision on stereopsis applies only to amblyopia ex anopsia associated with monocular strabismus, and does not apply to poor vision from other causes.

The observation that no patient with a visual acuity of 20/50 or worse in the amblyopic eye developed third degree fusion does not mean that a child with 20/70 or 20/50 vision in one eye cannot develop stereoscopic vision later in life. However, if he does so, the vision in the amblyopic eye must be better than 20/50 when the vision in the other eye reaches 20/20. Thus, the visual acuity of the two eyes cannot differ by more than two lines on the Snellen chart if third degree fusion is to be obtained on the tests used in this survey.

These observations agree with those of Anderson,[1,2] Cashell[5] and others, but they apparently disagree with those of Nordlöw,[25] who found stereoscopic vision in about one third of his patients when the visual acuity was 20/50 or less in one eye and 20/20 in the other with correction. Since all of his tests for stereopsis were done on the synoptophore, using relatively large targets, the apparent disagreement between his findings and those reported here may be attributed to the difference of the tests used.

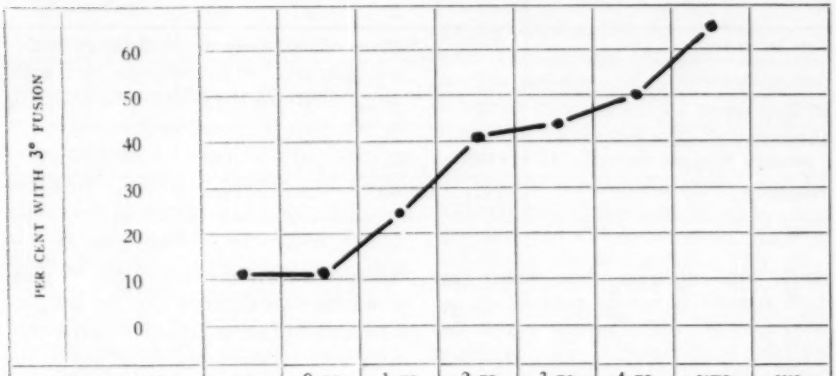
EFFECT OF AGE AT ONSET ON THIRD DEGREE FUSION

Because poor vision in one eye prevented postoperative third degree fusion in both constant and intermittent squint, all of the 80 patients who had one amblyopic eye with a visual acuity of 20/50 or worse were eliminated. The remaining 176 instances of patients with 20/40 or better vision were then tabulated to demonstrate the effect of the age at onset on the percentage of functional results obtainable. Table III shows that the percentage of functional results increased significantly as the age at onset increased. For example, when the onset occurred after the child was 5 years old, 66.6 per cent of the children developed third degree fusion; but when it occurred at birth, only 11.1 per cent did so. Hence, the age at onset was a potent factor in limiting the percentage of functional results obtained following surgical operation to correct strabismus.

Since only the patients with intermittent strabismus, and none with constant strabismus, developed third degree fusion when the strabismus was congenital, it is obviously futile to try to get a functional result when treating constant strabismus dating from birth. This observation is in agreement with those of Gibson,[16] Anderson,[1,2] Houlton,[17] Kempe,[18] Douglas[13] and Doggart,[12] all of whom have emphasized the poor prognosis for a functional result when treating constant strabismus dating from birth. Thus, even though Riise[26] reported third degree fusion following early operation on two patients with strabis-

TABLE III

EFFECT OF AGE AT ONSET ON THIRD DEGREE FUSION IN 176 CASES OF CONSTANT AND INTERMITTENT SQUINT WITH GOOD VISION IN EACH EYE



AGE AT ONSET OF SQUINT	AT BIRTH	0 TO 1 YR.	1 TO 2 YR.	2 TO 3 YR.	3 TO 4 YR.	4 TO 5 YR.	OVER 5 YR.	UN-KNOWN
No. of Cases	36	17	16	46	20	16	15	10
No. with 3°	4	2	4	19	9	8	10	4
Per Cent with 3°	11.1	11.7	25	41.3	45	50	66.6	40

mus occurring before either was 6 months of age, most observers would agree with Law,[19] who said that "with the rarest exceptions, a binocular result is never obtained when the deviation dates from birth."

However, since the age at onset had little or no effect on the percentage of functional results when the deviation was intermittent, one must concur with Lyle and Foley,[23] Cooper,[7,8] Costenbader[9] and Luhr and Schlossman[20] that the prognosis for a functional result is always good when the deviation is intermittent.

EFFECT OF DURATION OF SQUINT ON THIRD DEGREE FUSION

The duration of squint (DOS) may be defined for the purpose of this paper as the time interval between the age at onset and the age at operation, both of which have great prognostic significance for a functional result.

The duration of squint can be measured in units of time (months or years) or in terms of a percentage of the patient's lifetime. In the percentage method, the percentage is calculated as follows: If a constant squint began at birth, the DOS would always be 100 per cent; if it began at 3 years and was corrected at 4 years, the DOS would be 25 per cent (1 is 25 per cent of 4); if it began at 3 years and was corrected at 6 years, the DOS would be 50 per cent (3 is 50 per cent of 6). Table IV was designed to illustrate the relative merits of calculating the DOS by the unit of time method as against the percentage method for estimating the prognosis for a functional result in six children with a DOS varying from one to six years' duration, in all of whom a constant squint began at birth. One would expect that, everything else being equal, patient 1, with a DOS of one year, would have a better prognosis for third degree fusion than patient 6, with a DOS of six

TABLE IV

EFFECT OF THE DURATION OF THE SQUINT (DOS) ON THIRD DEGREE FUSION WHEN MEASURED IN YEARS OR IN A PERCENTAGE OF PATIENT'S LIFETIME

PATIENT	1	2	3	4	5	6
Age at onset	Birth	Birth	Birth	Birth	Birth	Birth
Age at operation	1	2	3	4	5	6
DOS in years	1	2	3	4	5	6
DOS in percentage of patient's lifetime	100	100	100	100	100	100
Prognosis	Poor	Poor	Poor	Poor	Poor	Poor

years. But experience has shown that the prognosis is equally poor in all, because patients with constant squint dating from birth rarely, if ever, develop a functional result, even when the deviation is fully corrected later in life.

Thus, since the DOS was 100 per cent in all when calculated by the percentage method, and since the DOS varied so much when measured by years, the percentage method gives a clearer picture of the prognosis for a functional result than does the unit of time method.

Many writers, including Cooper,[7,8] Gibson,[16] Lyle,[21] Cashell,[5] have emphasized that the prognosis for a functional result is poor when the operation is delayed until the patient is 6 years old or older. This statement is generally true but may be misleading unless the age at onset and the duration of the squint are considered. For instance, table V illustrates the vast difference of the prognosis for third degree fusion in seven children with constant squint, in whom the age at onset varied from birth (in patient 1) to 6 years (in patient 7), and on whom an operation was done to correct the squint at 6 years in each case. Experience has shown that, everything else being equal, cases 6 and 7 (with a DOS of 16.6 per cent and 0 per cent respectively) have an excellent prognosis for postoperative third degree fusion; cases 1 and 2 (with a DOS of 100 per cent and 83.3 per cent respectively) have a poor prognosis, and cases 3, 4 and 5 (with a DOS of 66.6 per cent to 33.3 per cent) have a fair to good prognosis. Since the age of the patient was the same at operation in all seven children, and since the prognosis for a functional result varied so much, it is clear that the

TABLE V

EFFECT OF THE DURATION OF THE SQUINT (DOS) ON THIRD DEGREE FUSION WHEN MEASURED IN YEARS OR IN A PERCENTAGE OF PATIENT'S LIFETIME

PATIENT	1	2	3	4	5	6	7
Age at onset	Birth	1	2	3	4	5	6
Age at operation	6	6	6	6	6	6	6
DOS in years	6	5	4	3	2	1	0
DOS in percentage of patient's lifetime	100	83.3	66.6	50	33.3	16.6	0
Prognosis	Poor	Poor	Fair	Good	Good	Excellent	Excellent

percentage method gives a more accurate estimate of the prognosis than does mere consideration of the age of the patient at operation.

The variable prognosis in these seven cases may be explained by assuming that any child who develops a constant squint at age five or later has a fully, or almost fully, developed fusion faculty which is not quickly lost; and that another child, whose squint began at the age of three, has an incompletely developed fusion sense which, because it is less than fully developed, deteriorates more quickly. In both instances binocular single vision with stereopsis can be re-established, provided the vision is good in each eye and the squint is fully corrected before it has existed too long. However, an infant with constant squint dating from birth has little or no fusion ability, and little or no chance of developing it later even though the deviation may be fully corrected early in life.

In trying to explain why these patients with constant squint dating from birth never developed third degree fusion, Worth[30] assumed the existence of a defective or absent fusion faculty as the primary cause. Chavasse,[6] however, declined to accept this idea and claimed that most infants with congenital squint would develop normal fusion if the deviation were fully corrected before 2 years. Several authors, among them Lyle[22] and Costenbader,[9] have endorsed this theory, but Morgan and Arstikaitis[24] and others have denied that the functional results are better with early operation. Despite the fact that Chavasse's theory has been widely accepted, there are to date no published reports to prove that this worthy objective has been accomplished in a substantial percentage of constant squints dating from birth.

EFFECT OF DURATION OF STRABISMUS ON THIRD DEGREE FUSION

When the 80 amblyopic cases were eliminated and the duration of the squint calculated by the percentage method, it became strikingly apparent that the duration of the squint had an enormous influence on the percentage of functional results obtained. Thus, of 138 patients with constant squint, only 1.9 per cent had a functional result when the duration was 75 per cent or more, while 56.2 per cent did so when the duration was 25 per cent or less (table VI). Consequently, it is evident that the prognosis for a functional cure was extremely poor when the duration was very long, but very good when it was very short. This opinion is shared by Lyle,[21] Douglas,[13] Gibson,[16] Cashell[5] and others.

When the deviation was intermittent, a long duration had a much less devastating effect on the functional results. In 38 such instances the percentage of functional cures was never less than 62.5 per cent, even when the duration was over 75 per cent (table VI). However, when the duration was shorter, the percentage of functional results increased only slightly, indicating that the duration had little or no retarding effect on the results in these instances. This conclusion confirms the opinion of other writers on the subject, among them Luhr and Schlossman,[20] Lyle and Foley,[23] and Costenbader.[9]

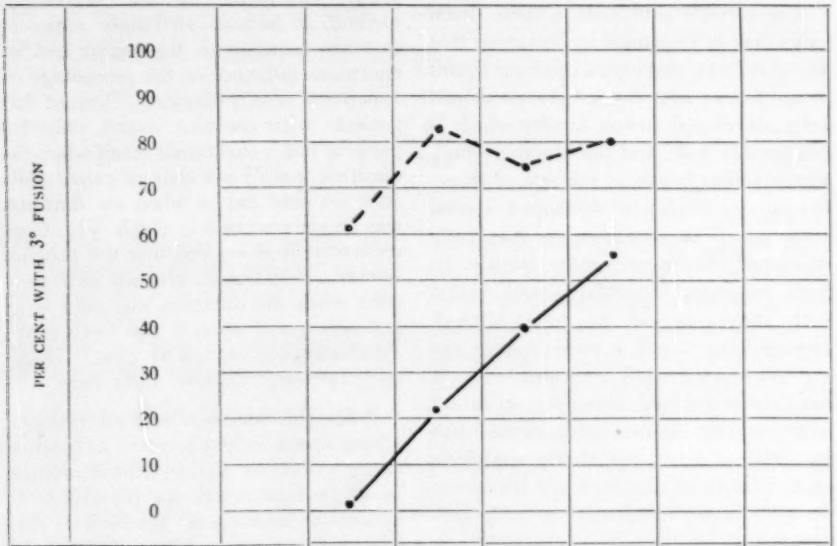
EFFECT OF RESIDUAL STRABISMUS ON THIRD DEGREE FUSION

In order to appraise the influence of a residual deviation on the functional results when the vision was good in each eye, the 38 patients with intermittent squint and the 138 patients with constant squint were analyzed separately.

When the squint was fully corrected, 100 per cent of the group with intermittent squint but only 66.6 per cent of the

TABLE VI

EFFECT OF DURATION OF THE SQUINT ON THIRD DEGREE FUSION IN 138 PATIENTS WITH CONSTANT SQUINT AND 38 PATIENTS WITH INTERMITTENT SQUINT WITH GOOD VISION IN EACH EYE



DURATION OF SQUINT (PERCENTAGE OF PATIENT'S LIFETIME)	75 TO 100	50 TO 75	25 TO 50	0 TO 25	UNKNOWN	TOTAL NUMBER
Number with constant squint	51	27	40	16	4	138
Number with 3° fusion	1	6	16	9	0	32
Per cent with 3° fusion	1.9	22.2	40.0	56.2	0	23.1
Number with intermittent squint	8	6	8	10	6	38
Number with 3° fusion	5	5	6	8	4	28
Per cent with 3° fusion	62.5	83.3	75.0	80.0	66.6	73.6

●——● = Percentage of constant squint with 3° fusion

●— — —● = Percentage of intermittent squint with 3° fusion

group with constant squint developed postoperative third degree fusion; but when a residual deviation persisted, only 41.1 per cent of the former and *none* of the latter got a functional result (tables VII, VIII). Therefore, it is clear that the percentage of functional results was always greater for both groups when the deviation was fully corrected, but was much reduced in the group with intermittent squint and completely abolished in the group with constant squint when a residual squint persisted. In other words, the prognosis for a functional result was always better in the group with intermittent squint, especially when the deviation was fully corrected; and always worse in the group with constant squint, particularly when a residual squint persisted.

TABLE VII

EFFECT OF RESIDUAL SQUINT ON THIRD DEGREE FUSION IN 38 PATIENTS WITH INTERMITTENT SQUINT WITH GOOD VISION IN EACH EYE

	WITHOUT * RESIDUAL SQUINT	WITH † RESIDUAL SQUINT	TOTAL NUMBER
Number of cases	21	17	38
Number with 3° fusion	21	7	28
Per cent with 3° fusion	100	41.1	73.6

* Less than 10△ of residual deviation (phoria or tropia)
† More than 10△ of residual deviation (phoria or tropia)

TABLE VIII

EFFECT OF RESIDUAL SQUINT ON THIRD DEGREE FUSION IN 138 PATIENTS WITH CONSTANT SQUINT WITH GOOD VISION IN EACH EYE

	WITHOUT * RESIDUAL SQUINT	WITH † RESIDUAL SQUINT	TOTAL NUMBER
Number of cases	48	90	138
Number with 3° fusion	32	0	32
Per cent with 3° fusion	66.6	0	23.1

* Less than 10△ of residual deviation (phoria or tropia)
† More than 10△ of residual deviation (phoria or tropia)

When the deviation was fully corrected and the duration of the squint was 50 per cent or less, 92.7 per cent of the group with constant squint developed third degree fusion, but only 36.8 per cent did so when the duration was over 50 per cent (table IX). Hence, the duration of a constant squint materially affected the results, even when the strabismus was fully corrected and the vision was good in each eye. Also, since none of these patients developed postoperative stereopsis in the presence of a residual squint, it is plain that the prognosis for a functional result in constant squint is good only when (1) the deviation is ful-

TABLE IX

EFFECT OF DURATION OF THE SQUINT AND OF A RESIDUAL DEVIATION ON THIRD DEGREE FUSION IN CONSTANT SQUINT

	DURATION OF THE SQUINT			TOTAL NO. OF CASES
	50% OR LESS	OVER 50%	UNKNOWN	
Number without a residual squint	27	19	2	48
Number with 3° fusion	25	7	0	32
Per cent with 3° fusion	92.6	36.8	0	66.6
Number with a residual squint	29	59	2	90
Number with 3° fusion	0	0	0	0
Per cent with 3° fusion	0	0	0	0

ly corrected, (2) the duration of the strabismus is 50 per cent or less, and (3) the vision is good in each eye. The poor prognosis for a functional result in constant squint when a vertical or a horizontal deviation remains has been amplified by Scobee,[27,28] Fink,[15] Spaeth,[29] Costenbader and Bair,[10] Anderson,[3] Brown,[4] Cushman,[11] and Dowler.[14]

However, the duration of the squint had no apparent influence on the percentage of functional results obtained in the group with intermittent squint when the squint was fully corrected, and little or no effect when a residual deviation persisted (table X). Accordingly, it would seem that the percentage of functional results in intermittent squint depended almost entirely on full correction of the deviation. This observation is in general agreement with other opinions regarding the prognosis for a functional cure in the surgical treatment of intermittent squint.

DISCUSSION

Because the date of onset (as given by the parents), the visual acuity and the degree of fusion (as described by the patients), and the amount of squint (as measured by the examiner) are all subject to human error, any conclusions based on this clinical study must be, at best, only approximately correct. Also, it is obvious that the number of cases in some of these tables was too small to have statistical significance. This deficiency occurred because it was necessary first to eliminate the 80 patients with amblyopia and then to classify the remaining patients as to the nature of the squint (constant or intermittent), the duration of the strabismus and the amount of residual deviation present. In this connection, Lyle and Foley[23] and Douglas[13] have emphasized that statistics on the functional results in the treatment of squint are quite meaningless and illegitimate, unless the nature of the case and the age at onset are considered.

Despite these shortcomings, the general conclusions reached on the basis of these data have received general confirmation in the form of three excellent similar surveys reported in the past two years. Thus, in a critical analysis of 287 patients with nonparalytic convergent strabismus, Lyle and Foley[23] found that only 11 per cent of the nonaccommodative group developed full binocular single vision after operation, and that the prognosis for a functional result in constant squint was always poor when the age at onset was early and the duration of the squint was long, even though extensive orthoptic treatment was given and the deviation fully, or almost fully,

TABLE X

EFFECT OF DURATION OF THE SQUINT AND OF A RESIDUAL DEVIATION ON THIRD DEGREE FUSION IN INTERMITTENT SQUINT

	DURATION OF THE SQUINT			TOTAL NO. OF CASES
	50% OR LESS	OVER 50%	UNKNOWN	
Number without a residual squint	12	6	3	21
Number with 3° fusion	12	6	3	21
Per cent with 3° fusion	100	100	100	100
Number with a residual squint	6	8	3	17
Number with 3° fusion	2	4	1	7
Per cent with 3° fusion	33.3	50	33.3	41.1

corrected. They added that early operation to correct congenital squint should produce better functional results than those reported, but they supplied no data to substantiate this theory. Nordlöw[25] reported 70 patients with permanent convergent squint, of which 59.4 per cent developed stereopsis after one, two or three operations, when the age at onset was between 6 months and 7 years and the duration of the squint varied from six months to five and a half years. He stressed the importance of early operation in achieving a functional result in constant convergent squint beginning at 6 months of age or later. Cooper[7,8] reported 27.1 per cent functional cures in 382 patients with nonaccommodative concomitant esotropia and in 71.2 per cent of 101 patients with concomitant exotropia following surgical operation, with and without the aid of orthoptic exercises. He stated that the percentage of functional results was greater when the vision was good in each eye, when the squint began after 18 months of age, and when it was corrected early in the life of the child. His criterion for a functional result did not include tests for stereoscopic vision because some of his patients were too young for such tests.

A valid comparison of the functional results obtained by these authors and those achieved in this survey cannot be made from the data available, chiefly because the criteria for a functional result were not uniform. Despite these differences, however, all four surveys showed conclusively that the age at onset, the duration of the squint, the visual acuity and the nature of the deviation (constant or intermittent) all played a significant role in determining the percentage of functional results accomplished by surgical operation to correct strabismus.

CONCLUSIONS

1. The prognosis for a functional result in constant strabismus was always poor under the following circumstances:
   a. The corrected vision in one eye was 20/50 or worse and that in the other eye was 20/20 or better.
   b. The strabismus began at birth.
   c. The duration of the strabismus was very long.
   d. A residual esotropia or exotropia of over 10 prism diopters or a residual hypertropia of over 2 prism diopters existed in the primary position.
2. The prognosis for a functional result in constant strabismus was good only under these circumstances:
   a. The vision in the amblyopic eye was 20/40 or better when the vision in the fixing eye was 20/20.
   b. The strabismus began after birth.
   c. The duration of the strabismus was short.
   d. The horizontal deviation was corrected to 10 prism diopters or less and the vertical to 2 prism diopters or less in the primary position.
3. The prognosis for a functional result in intermittent strabismus was always favorable when the vision was good in each eye, even though strabismus had existed for a long time.

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DISCUSSION

FRANK D. COSTENBADER, M.D., Washington, D. C.: I would like to commend Dr. Berke on the excellence of his paper and especially to thank him for the unusual privilege of receiving his paper many weeks ago. This has given me the opportunity to critically compare his and my experiences.

I have reviewed several hundred unselected cases, but unfortunately have obtained only 114 roughly comparable to those cited by the author. The qualifications have been that all patients must have a postoperative final alignment of within 10 prism diopters of straight, and that adequate tests for binocular vision should have been done subsequently. While the arrow test for gross stereopsis and the Keystone DB for refined graded stereopsis were used on only a limited number of patients, the Wirt fly test and the Wirt graded stereopsis test were used on most of them, and the Worth four dot test on all.

I am in full agreement that the presence of stereopsis would seem to be the major quality in evaluating the attainment of a *perfect* result in surgical procedures to correct squint.

However, while perfection is the ultimate goal in any endeavor, I cannot agree that lesser degrees of success are not worth while if perfection cannot be attained, as is implied though not so stated by Dr. Berke. Thus, while stereopsis, as demonstrated by the stereoscope or polaroid devices, gives evidence of a high degree of success and stability resulting from surgical procedures to correct squint, binocular single vision as demonstrated by the Worth four dot test, or a tendency to restore alignment after removing cover is evidence of a significant though lesser degree of stability. I thoroughly agree that the presence or absence of stereopsis on the major amblyoscope does not give evidence of its existence in daily life and should not infer a cure. However, the presence of fusion with stereopsis as demonstrated on the major amblyoscope is of prognostic significance, and gives hope of a cure if accurate alignment can be attained.

Of 530 unselected private patients with strabismus who were operated upon and had sufficient postoperative findings to justify analysis, 114 (22 per cent) had straight eyes and a visual acuity of 20/40 or better. These patients are considered in further discussion.

I would agree that amblyopia of significant degree is a bar to the ultimate attainment of fusion with stereopsis, but I cannot accept visual acuity of 20/50 or poorer as being an absolute barrier. We have, in our series, one patient who has a 20/50 visual acuity, one with 20/60, and one with 20/70, all of whom have a high degree of stereopsis, and two patients whose visual acuity is 20/70 and who obtain gross stereopsis. I have not used these cases in our further considerations.

Dr. Berke has recognized the fact that history of onset of strabismus cannot always be obtained with accuracy. With this fact I would agree, and add emphasis, since it has an important bearing on the duration of squint (DOS), which has been suggested as a factor in the cure of strabismus. It is common knowledge that infant eyes are frequently unstable the first three or four months of life, that infant features often give an appearance of strabismus which subsequently cannot be confirmed by cover test, and that parents are notoriously inaccurate observers.

In an effort to determine the significance of the age at onset, the entire series of 530 patients were studied. Of these, 330 had a constant heterotropia which had been apparent since birth, while 200 patients had an intermittent or constant heterotropia which became evident at some time after birth.

Of the 330 patients with constant heterotropia, only 32 (10 per cent) had a final deviation of 10 prism diopters or less, and good vision in each eye. Of these, one had 85 per cent stereopsis, two had 30 per cent stereopsis, and seven had stereopsis of less than 30 per cent. In addition, 11 patients had Worth four dot fusion but no stereopsis, and an additional 15 patients maintained straight eyes but no fusion on any of the clinical testing methods used. These facts would suggest two things. First, there are patients with constant strabismus from birth who do have stereopsis, though the number is small. I have the impression that very early operation (during the first 6 to 12 months of life) and good alignment do result in functional cure at times. Second, some patients exhibited no stereopsis but did maintain continuous good alignment. Thus, tests other than those for stereopsis have some significance.

When the 200 patients in whom squint definitely developed some time after birth are considered, it becomes very evident that the prognosis for cure is considerably better than in the congenital group. Eighty (40 per cent) patients had straight eyes and good vision. Of the patients who developed strabismus during the first year of life, 55 per cent had good stereopsis and 91 per cent had some degree of stereopsis. When considering those patients who developed strabismus after the first year of life, I found that 61 per cent had good stereopsis and 94 per cent had some stereopsis. It should be recognized that this rather high percentage of patients with stereopsis is probably due to the fact that many of them had intermittent deviations.

Evidently, while the presence of strabismus at birth does not preclude binocular single vision, even with stereopsis, the percentage of such cures increases abruptly when onset is some time after birth. We might speculate that both the early opportunity for binocular single vision and a fair to good fusion potential are factors in the later redevelopment of fusion when strabismus is corrected.

I will fully agree with the author that the duration of squint is a most significant factor in the cure of strabismus, and that the percentage method is a more valid method of calculation than that of the unit of time. As already pointed out, we have obtained some functional cures among people with congenital esotropia, so that even though the DOS is 100 per cent, the prognosis is not hopeless, though by no means favorable.

When estimated in terms of duration of squint by the percentage method, my findings

are similar to Dr. Berke's. Of those patients with squint (intermittent and constant) which had existed for 25 per cent of the life span but were corrected by operation, almost all had some degree of stereopsis. Of those patients with squint existing more than 25 per cent but less than 50 per cent of the life span, 50 per cent had stereopsis. However, at variance with Berke's findings was the fact that 50 per cent of those cases of squint existing from 50 per cent to 75 per cent of the life span also attained stereopsis. Again, in accord with the author, of those whose deviation had existed for 75 per cent of the life span, or more, few had stereopsis. Thus, we can confirm the author's general conclusions but feel that no valid distinction can be made in the prognosis of those whose strabismus has existed from 25 per cent to 75 per cent of the patient's life.

I am in full agreement with the statement that the prognosis for functional cure in intermittent strabismus is much better than that in constant strabismus, regardless of the duration. An analysis of our series shows that a high percentage of patients with intermittent exotropia, and a somewhat smaller percentage of patients with accommodative esotropia, demonstrate good fusion with stereopsis, as compared with a much smaller percentage of patients with acquired constant strabismus, and an even smaller percentage of patients with congenital constant strabismus. The opportunity for fusion is a prime factor in its maintenance. It is this premise (the most constant opportunity for fusion) which has led us to urge bifocals and, more recently, miotics in the maintenance and treatment of accommodative esotropia.

Two of Dr. Berke's qualifications seem open to question or clarification. He states that all cases in which the patient needed a second operation were considered failures. It would appear that he is being unduly harsh on himself, since many patients in our series obtained a functional cure after a second operation, and a few after a third or fourth. Critical analysis after whichever operation gives a good result seems entirely justified.

The other matter of some concern to one interested in orthoptics is the content of two statements. I quote: "Factors of little or equivocal importance were . . . the number of orthoptic exercises given. . . ." and "Active orthoptic treatment was rarely given for amblyopia or suppression." I must point out that if one is interested in obtaining fusion with stereopsis, nothing could be more important than the overcoming of suppression. While statistical evidence is not easily gathered, it is my considered opinion that intelligent orthoptics will greatly aid in overcoming suppression. And such orthoptics must not be measured in terms of the number of treatments, or the number of instruments used, but rather in terms of creating an awareness of two visions, i.e., diplopia.

Summary

1. I would agree with the author on the following points:
   a. Onset of strabismus at birth offers a poor prognosis for functional cure.
   b. Significant amblyopia precludes cure.
   c. The presence of a vertical deviation makes cure additionally difficult.
   d. The prognosis for an intermittent deviation is much better than that for a constant one.
   e. A residual constant deviation precludes functional cure.
2. I disagree with the following points:
   a. No congenital strabismus can obtain a functional cure.
   b. Visual acuity of less than 20/40 absolutely precludes cure.
   c. Orthoptics is of no value in obtaining a functional cure.
3. I would offer the qualifying thought that while cure with stereopsis is the ultimate goal, straight eyes with lesser degrees of binocular single vision are highly desirable.

DR. BERKE: I would like to thank Dr. Costenbader for taking the trouble to analyze such a large number of patients and for discussing this paper. I am happy to note that he agrees that the visual acuity, the age at onset, the duration of the squint, and the amount of residual deviation are all important factors in determining the percentage of functional results in surgical procedures to correct squint. It is particularly significant that we both arrived at essentially the same conclusions in view of the fact that he used a different test for stereopsis and analyzed his cases in a slightly different way. Also, he did not divide the constant from the intermittent cases in all of his groups nor were his cases all consecutive. Thus it is obvious that two observers working toward the same end can achieve very much the same conclusions by slightly different methods.

However, Dr. Costenbader disagrees with three or four of the minor points I made in the paper. For example, he found that 3 per cent of his 330 patients with constant squint

dating from birth (a truly remarkable number) developed stereopsis, while I found that none of my cases did so. I believe this small difference has little or no significance, because these figures are based on the observations of the parents. What is important is the observation that any patient with constant squint dating from birth always has a poor prognosis for a functional result.

In his wide experience Dr. Costenbader has found only 5 patients who developed stereopsis with 20/50 or 20/70 vision, while I found that none of my 80 patients did so. Here again I feel that this observation is not particularly significant when we realize that his tests for stereopsis were slightly different from mine and that the visual acuity as reported in children is not always 100 per cent accurate. The important observation is that amblyopia plays an important role in preventing postoperative stereopsis.

Dr. Costenbader thinks that I have not given orthoptic exercises the credit they really deserve. In the paper I say that such exercises played a minor role in determining the percentage of functional results. And so they did, when compared to such important factors as the visual acuity, the age at onset, the duration of the squint, and the amount of residual deviation present.

Dr. Costenbader believes that we should always strive for a functional result and, if we cannot get a perfect result, we should be satisfied with something less than perfection. I think that we all agree with him there, but I see no purpose in grouping these two types together or in downgrading the standard for a functional result. If we must have a first grade and a second grade and a third grade functional result, let us set up a standard for these three functional results; then when we report our results let us specify what type of a functional result we are talking about.

I have enjoyed Dr. Costenbader's discussion very much, and I would like to thank him again for bringing to us his rich experience in this fascinating and sometimes frustrating branch of ophthalmology.

INCIDENCE AND DETECTION OF GLAUCOMA BY ROUTINE TONOMETRY

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Detection of glaucoma at the earliest moment possible in its development should be the diagnostic objective in order to afford the greatest opportunity for successful treatment. Attainment of this objective requires inclusion in the ophthalmologist's diagnostic routine of investigations which will disclose a high percentage of glaucoma cases and still be practical for clinical use. The word "glaucoma" as used in this paper refers to the chronic simple (open angle) type. Secondary, absolute, and congenital glaucoma do not present as significant a problem in detection because their symptoms are usually more obvious. Detection of angle closure glaucoma is also dependent chiefly on methods other than tonometry.

The steps recommended by Kronfeld[6] for the diagnosis of early, wide angle glaucoma are, briefly, (1) history, (2) ophthalmoscopic study, (3) digital tonometry followed by instrumental tonometry unless tactile tension is definitely "soft," (4) field study, and (5) provocative tests. The minimum requirements for the early detection of glaucoma recommended by the Committee on Glaucoma[11] of the National Society for the Prevention of Blindness include slit lamp microscopy, gonioscopy and tonography in addition to the procedures mentioned above.

We propose that these recommended studies be divided into two groups, primary and secondary. Those in the primary group should be carried out on all patients over the age of 40. This group would include (1) history, (2) ophthalmoscopy, (3) instrumental tonometry (digital tonometry is not sufficiently reliable), and (4) slit lamp microscopy. The secondary group would consist of (1) visual field studies, (2) provocative tests, (3) gonioscopy, and (4) tonography. These tests would be utilized whenever the presence of an abnormality has been indicated by a test in the primary group.

The mechanistic theory of chronic simple glaucoma proposes that the initial alteration in ocular physiology is a decrease in the facility of aqueous outflow from the anterior chamber, resulting in increased intraocular pressure. During the early stages this increased pressure is seldom sufficient to produce corneal edema or glaucomatous pulsation of the retinal arterioles. Permanent characteristic visual field changes and cupping of the optic nerve develop gradually during the course of persistently increased intraocular pressure. The logical conclusion, therefore, is that measurement of the intraocular pressure (or the facility of aqueous outflow) must be performed routinely if glaucoma is to be detected prior to the development of optic nerve and visual field changes. Tonometry, being a relatively simple and rapid procedure, is the test of choice for this purpose rather than the more complicated and time consuming performance of tonography.

Accepting the validity of the foregoing statements, one would assume

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tonometry to be a routine part of every ocular examination of patients in an age group where glaucoma is most prevalent. A sampling of board certified ophthalmologists — to be presented later — revealed that one third did not perform this test routinely. Physicians less familiar with the glaucoma problem undoubtedly utilize tonometry much less frequently.

Establishment of the practice of routine tonometry by every ophthalmologist is, however, only the initial step in the program of glaucoma detection. Kurlander[9] has pointed out that there are 59 million Americans over 40 years of age. If every member of this group were to undergo tonometry by an ophthalmologist, each ophthalmologist would have to test about 8,000 individuals, obviously an impossible assignment. Several solutions to this problem have been suggested. One is mass screening, such as has been carried out in Philadelphia[2] and Cleveland.[14] Others[3,5,9,15] have suggested that tonometry be performed by general practitioners and internists routinely as a part of every general physical examination. Adoption of either or both of these methods of glaucoma detection would require the wholehearted assistance and cooperation of the entire ophthalmologic profession.

The present study reports the findings of routine tonometry in 2,000 patients over 40 years of age in an average ophthalmologic practice and the results of more detailed study of those having a tension of 25 mm. Hg or more (Schiøtz). Practically all tests were conducted with an electronic tonometer, using the 1954 conversion table of Friedenwald. Excluded from the study were all patients with previously diagnosed glaucoma, any ocular inflammatory condition, or ocular disease of any type which might be expected to alter intraocular pressure. These exclusions automatically eliminated patients with absolute, secondary, congenital, or acute angle closure glaucoma. All patients investigated were found to have open angles as far as could be determined by slit lamp and gonioscopic examination. One might suspect that an occasional patient in the chronic phase of angle closure glaucoma would be found in such a survey, but none was observed. Fifty-two individuals (2.6 per cent) were found to have intraocular pressure of 25 mm. Hg or more in at least one eye. These patients were divided into two groups on the basis of ophthalmoscopic and visual field studies. Designated as group A were those having glaucomatous field changes and/or cupping of the optic disc. The findings in this group were considered adequate to make a diagnosis of chronic simple glaucoma without further study. Group B included the remainder, i.e., those without either ophthalmoscopic or visual field abnormalities characteristic of glaucoma. Additional investigation of the patients in group B was carried out in an effort to establish the presence or absence of chronic simple glaucoma. Selection of the procedures used warrants a brief discussion.

Tonography and/or provocative tests are most commonly employed for this purpose, and their merits have been investigated extensively. Tonography has not, as yet, become a procedure suitable for use by the average ophthalmologist. Kronfeld[8] stated that tonography "was not an easy procedure and had many potential sources of error," and that "the procedure should be reserved for clinics where details of the technique were fully mastered." Spencer, Helmick and Scheie[13] enumerated the possible sources of error in technique and reported several difficulties encountered with equipment. Correction of these difficulties required assistance not available to most ophthalmologists. Furthermore, in the establishment of their

tonographic laboratory, these authors had the benefit of a visit to the laboratory of Dr. M. W. Grant and of his personal advice. For these reasons provocative tests were considered more satisfactory for use by the average ophthalmologist and were selected for our investigation.

Leydhecker[10] recommended the water drinking test of Schmidt as the first to be employed in the investigation for chronic simple glaucoma. This test has the advantages of simplicity and a high index of reliability. A rise in intraocular pressure of 6 mm. Hg or more, as suggested by Kronfeld,[7] was chosen as the criterion for indicating the presence of glaucoma. Becker and Christensen[1] found that on this basis 42 per cent of a group of known glaucomatous eyes gave a positive response. Scheie, Spencer and Helmick,[12] however, found the test 96 per cent accurate under similar circumstances. They also expressed the opinion that "tonography does not seem to be as reliable a diagnostic test in chronic simple glaucoma as the water provocative test." Nineteen patients (.95 per cent) with either a positive result on the water provocative test or an intraocular pressure of 32 mm. Hg or more on two occasions were considered to have glaucoma and were classified in group B-1. This resulted in a diagnosis of glaucoma in 35 (67.4 per cent) of the 52 patients with an initial pressure above 24 mm. Hg. Seventeen patients (.85 per cent) not meeting either of these standards were regarded as nonglaucomatous and were classified as group B-2. Included in this group were a few patients in whom the follow-up study was incomplete. Although group B-2 has been designated as "nonglaucomatous," we recommended that the patients in this group return at intervals of three to six months for further tonometry and other studies as would appear indicated. (During the ensuing year, two of the 17 patients in this group were found to have sufficient evidence for a definite diagnosis of glaucoma.)

Consideration of the usefulness of routine tonometry as a diagnostic procedure would not be complete without recognition of the source of possible error. The well known phase variations of pressure, and the not infrequent remission of pressure, in chronic simple glaucoma suggest at once that a certain number of patients with glaucoma would pass through a routine test at a time when their pressure was below 25 mm. Hg. This group might be regarded as having a "false negative" response to tonometry. The frequency of this occurrence is difficult to determine. Becker and Christensen,[1] reporting on a group of 188 eyes with known glaucoma selected for tonographic study, found only 39 per cent with intraocular pressure of 24 mm. Hg or above after three days without treatment. Scheie, Spencer, and Helmick[12] in selecting a similar group of 162 eyes for study found the intraocular pressure of all to be 30 mm. Hg or higher. In our survey, 6 patients (.3 per cent) with tension below 25 mm. Hg were suspected of having glaucoma because of the appearance of the optic discs. The diagnosis in these cases was confirmed by field studies and/or provocative tests and tension studies. Even more difficult to detect were patients in the "preglaucoma" state, i.e., patients in whom fundus and field changes had not yet developed and who were examined during a phase variation resulting in an intraocular pressure below 25 mm. Hg. In our study, 3 patients (.15 per cent) of this type were brought to our attention subsequently, having had a normal tension initially. One may only speculate as to how many others there may have been. Therefore, a total of 9 patients (.45 per cent) with glaucoma had, at the time of original tonometry, intra-

TABLE I

RESULTS OF A SURVEY OF 2,000 PATIENTS OVER FORTY YEARS OF AGE IN AN AVERAGE OPHTHALMIC PRACTICE USING TONOMETRY ROUTINELY

	NUMBER OF PATIENTS	PERCENTAGE OF TOTAL PATIENTS EXAMINED	PERCENTAGE OF PATIENTS WITH PRESSURE ABOVE 24 MM. HG
Intraocular pressure above 24 mm. Hg in one or both eyes	52	2.60	100
Group A: Intraocular pressure above 24 mm. Hg plus field and/or fundus changes	16	0.80	30.8
Group B-1: Intraocular pressure above 24 mm. Hg and positive water test or repeated pressure of 32 mm. Hg or higher, but no field or fundus changes	19	0.95	36.6
Total glaucoma cases with initial pressure above 24 mm. Hg	35	1.75	67.4
Group B-2: Intraocular pressure above 24 mm. Hg but water pressure negative, intraocular pressure below 32 mm. Hg and no field changes	17	0.85	32.6
Cases with other evidence of glaucoma but initial pressure below 25 mm. Hg	6	0.30	
Cases subsequently diagnosed as glaucoma, with initial pressure below 25 mm. Hg and no fundus or field changes	3	0.15	
All glaucomas	44	2.20	

TABLE II

ANALYSIS OF 44 CASES OF GLAUCOMA

		NUMBER	%
Initial pressure above 24 mm. Hg		35	80
Initial pressure below 25 mm. Hg		9	20
Optic nerve and/or glaucomatous field changes present		22	50
Optic nerve and/or glaucomatous field changes not present		22	50
22 cases with field or disc changes	(Tension above 24 mm. Hg)	16	73
	(Tension below 25 mm. Hg)	6	27
22 cases without field or disc changes	(Tension above 24 mm. Hg)	19	86
	(Tension below 25 mm. Hg)	3	14

ocular pressure below 25 mm. Hg. Results of the survey classified on the above basis are found in table I.

It will be observed that by various means a diagnosis of glaucoma was made in 44 (2.2 per cent) of the patients tested. Analysis of these 44 cases reveals that a total of 35 (80 per cent) had an initial intraocular pressure of 25 mm. Hg or higher, while 9 (20 per cent) had an intraocular pressure of less than 25 mm. Hg (table II). This would suggest that the accuracy of mass screening surveys utilizing tonometry would not exceed 80 per cent. Of further interest from a statistical point of view is that of the 44 cases of glaucoma exactly 50 per cent had optic nerve and/or glaucomatous field changes and 50 per cent did not. Of the 22 cases with optic nerve and field changes, 16 (73 per cent) had an initial pressure of 25 mm. Hg or higher, while 6 (27 per cent) had an initial pressure below 25 mm. Hg. By comparison, in the 22 cases without optic nerve or field changes, 19 (86 per cent) had an initial pressure of 25 mm. Hg or higher, and 3 (14 per cent) had an initial pressure of less than 25 mm. Hg. The percentages in this latter group are obviously misleading because of the difficulty in arriving at a diagnosis of glaucoma in a patient with so-called normal intraocular pressure and no fundus or field changes.

A survey of 2,000 patients somewhat similar to this, conducted by Hildreth and Becker,[4] revealed 49 (2.45 per cent) with findings similar to those in our group B (36, or 1.8 per cent). Tonography with water drinking resulted in a diagnosis of glaucoma in 72 per cent of their series, while the water drinking provocative test alone resulted in a diagnosis of glaucoma in 53 per cent of ours. Whether this difference indicates a greater sensitivity of their diagnostic technique is not clear, since comparative data within each survey are not available.

To evaluate the prevalence of the use of routine tonometry by ophthalmologists certified by the American Board of Ophthalmology, questionnaires were sent to 200 members. One hundred seventy-five of these were returned. The replies have been classified, inserted, and underlined (table III). The results of our survey, when applicable, have been included for comparison. Approximately two thirds of those replying indicated that they use tonometry routinely, and 65 per cent had been doing so for more than seven years. Among those who did not utilize tonometry routinely, the replies regarding the methods used for glaucoma detection were so varied that a statistical summary was impossible. The majority, however, relied on ophthalmoscopic examination and tactile evaluation of tension. Several of these commented that although the accuracy of tactile evaluation of tension would be variable, each ophthalmologist would have to determine the reliability of his own judgment by comparison with instrumented tonometry. We would suggest that each one who places reliance on this method has the obligation of proving to himself his own accuracy. To those who rely chiefly on the ophthalmoscope, we would point out that 50 per cent of the glaucoma patients in our series did not have visible glaucomatous changes in the optic nerve. Furthermore, our diagnostic objective is to detect glaucoma prior to the development of such changes, if possible. On the other hand, ophthalmoscopic examination should not be neglected, since 27 per cent of the cases with glaucomatous cupping of the optic discs had intraocular pressure of less than 25 mm. Hg on the initial test. Visual field studies are of the utmost importance in the diagnosis and management of glaucoma and should be per-

TABLE III

Do You Utilize Routine Tonometry?	YES	NO
	68%	32%

If answer to the above is YES please answer the following questions:

1. How long have you done so?

1-3 years	4-6 years	7+ years
11%	24%	65%

2. What age or other limitations do you place on the procedure?

Age 20 and above	Age 30 and above	Age 40 and above
13%	23%	64%

3. What per cent of the patients tested are found to have above normal intraocular pressure? (Estimate)

Less than 2%	2%-4%	5%-7%	8% and up	2.6%
48%	36%	9%	7%	Our survey

4. Approximately what per cent of those with increased pressure have no other apparent evidence of glaucoma?

25%	50%	75%	100%	33%
45%	31%	22%	2%	Our survey

(Figures underlined are percentage of replies corresponding to adjacent figure.)

5. Approximate number of years in practice of ophthalmology

Less than 10	11-20	21-30	30 plus
33%	41%	23%	3%

If answer to the above is NO please answer the following questions:

1. Do you believe that routine tonometry would disclose a significant number of patients with increased intraocular pressure which would not be detected by other methods of examinations?

YES	NO
43%	57%

2. On what diagnostic procedure do you rely most frequently to detect chronic simple (open angle) glaucoma?

Ophthalmoscope Visual fields Tactile tension
History Other (specify)

3. Approximate number of years in practice of ophthalmology

Less than 10	11-20	21-30	30 plus
29%	45%	21%	5%

formed when any suspicion of glaucoma exists, but they are not suitable for routine use in the detection of glaucoma. A primary objection to their use is the time factor; furthermore, it is doubtful whether many patients with glaucomatous field defects have both normal ophthalmoscopic findings and normal intraocular pressure. For these reasons this test (visual field study) has been assigned to the secondary group. It would also appear that provocative tests, gonioscopy, and tonography are not practical for routine use but should be utilized when indicated by findings from the primary test group.

The use of routine tonometry presents certain problems which should not be overlooked. Chief among these is the anxiety engendered by the use of an unfamiliar procedure and, more particularly, by the finding of a borderline tension. In such cases the physician may be unable to assure the patient that he does *not* have glaucoma. In spite of the most careful management of this problem, a certain amount of iatrogenic anxiety seems unavoidable. It is equally important that care be exercised not to inform the patient that he *has* glaucoma until the diagnosis is firmly established. This caution may unavoidably necessitate a considerable period of observation, testing, and anxiety for the patient, but this is preferable to making a diagnosis of glaucoma when it does not exist. In our experience it is virtually impossible to convince a patient who has received an erroneous diagnosis of glaucoma (usually hastily made) that he does not have the disease.

A second problem of some magnitude is the reassurance which some people mistakenly derive, despite explanation, from a single normal tonometric reading. Just as one elevated intraocular pressure reading does not mean glaucoma, it must also be recognized that one normal reading does not exclude glaucoma. In practice, these problems, rather than the actual tension taking, exercise the greatest demand on the physician's time. Should mass screening for glaucoma and routine tonometry by non-ophthalmologists become widespread practices, these problems will undoubtedly be considerably more frequent.

The possibility of transmitting ocular infection or causing significant corneal damage by tonometry has been suggested. To our knowledge neither of these complications occurred in this study.

SUMMARY

1. Routine tonometry, with additional diagnostic studies when indicated, disclosed 35 (1.75 per cent) cases of previously undiagnosed chronic simple glaucoma in 2,000 patients with otherwise normal eyes. Glaucoma was discovered in an additional 9 patients (.45 per cent) by methods other than tonometry. The total incidence of glaucoma was 2.2 per cent. In 19 (43 per cent) of these 44 cases of glaucoma the diagnosis was made on the basis of intraocular pressure of 32 mm. Hg or higher and/or a positive response to the water drinking test in the absence of demonstrable visual field defects.

2. Diagnostic studies recommended for glaucoma detection have been divided into primary and secondary groups. The primary group is recommended for routine use in patients over the age of 40, and the secondary group for use when indicated by the findings from the primary group.

3. A survey relative to the use of routine tonometry by ophthalmologists was made and the results reported.

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DISCUSSION

BRUCE L. KANTAR, M.D., Minneapolis: I want to congratulate Dr. Porter on his efforts to add to our knowledge by his survey and report. In the literature from 1951 on, there are surveys from Philadelphia, Cleveland, California, Oregon, and Finland, among others. These are published variously in the Journal of the American Medical Association, ophthalmology journals, Sight-Saving Review, Public Health Reports, and other journals. Each survey on this general subject makes its own interesting points, but two things are apparent from all these surveys:

1. Simple glaucoma is a real public health problem and will become increasingly so as our population continues to live longer.
2. Routine and repeated tonometry is the best diagnostic tool for early detection of simple glaucoma.

As you might have suspected by now, I have a survey to report also. Our survey was done in the first six months of 1955 at the University of Minnesota Medical School when one senior medical student in a clerkship group said he doubted the reported 2 per cent incidence of undiagnosed simple glaucoma in people over 40 years of age in the United States. This student and five others decided to learn tonometry and check the incidence in their patients. Although in their extra time they did tonometric tests on 684 patients, follow-up studies and complete data were available on only 453 outpatients at University Hospitals. We shall limit the report to them. We used a screening level of 30 mm. Hg (Schiøtz) or more, and also asked the seniors to report any patient with a difference of 10 mm. Hg or greater between the two eyes. Twenty patients were singled out, and further investigations were carried out at University of Minnesota Hospitals Eye Clinic. The results on the investigation of 8 of these patients were definitely positive, and on 3 they were suspected positive, for chronic simple glaucoma. Thus, with an accuracy between 40 and 50 per cent, our two interested senior medical students screened out patients with simple glaucoma by means of tonometry. I think a direct outcome of all these surveys and of this local effort is that the University of Minnesota outpatient department is now happy to have senior medical students include tonometry as a part of the routine physical examination. I think this is one absolutely necessary step if doctors other than ophthalmologists are to help in glaucoma case findings. I am sure that you cannot get a significant number of men already in general medical practice to take up tonometry and incorporate it into their examination routines. They may agree with what we say, but they have their own problems to take care of.

Some of the conclusions our seniors reached seem interesting.

1. They thought ophthalmologists should all do tonometry, too, and from what they could determine, this was not the case. Dr. Porter touched on this in discussing results of his questionnaire—one third of Board certified ophthalmologists do not do it. Apparently all too often a tonometer is used to verify the presence of that which is palpated instead of to detect what the fingers cannot feel. For those who agree that palpation may be inaccurate, except when it is their own fingers feeling those eyeballs, Dr. Porter's advice to check yourself and your palpation against your own tonometer is excellent. I think that as medical doctors we should use all the medi-

cations and instruments we alone are privileged to use in our efforts to make a diagnosis and help our patients.

2. They thought tonometry was easier to do than ophthalmoscopy. Dr. Porter's paper pointed out that half the glaucoma patients in his series did not have visible glaucomatous changes in the optic nerves. Also, in the very excellent Philadelphia study, except for one case, no case of glaucoma was diagnosed by ophthalmoscopy that tonometry did not also pick up. Certainly as far as glaucoma is concerned, our future medical doctors should be given the best instruction for detection of this disease.

3. One student felt that tonometry should be done in a routine physical examination just as much as, for example, a routine proctoscopy, which they are all taught should be done. I do feel that 25 mm. Hg from all available data is a much better screening level than the 30 mm. Hg we used.

Dr. Porter includes tonography in his secondary group of diagnostic studies. Tonography is not available to me or my patients in Minneapolis. I have no working knowledge of tonography and leave a discussion of its merits to those who are experienced with it. In my diagnostic group, therefore, I would include what to me is the most helpful and valuable form of routine and repeated tonometry; namely, the measurement in glaucoma suspects and in patients with borderline tensions, as well as in patients under active miotic treatment, of the phasic variations in ocular tension occurring throughout the day. This instability of tension is an early characteristic of simple glaucoma and becomes more and more pronounced as the disease progresses. According to Duke-Elder, exaggerated diurnal variations of intraocular pressure are one of the most fundamental aspects of the disease. I think these studies should be combined with the others already listed by Dr. Porter.

With widespread use of routine tonometry and further investigation to evolve better screening methods, if there are any, we will find more patients with glaucoma and also more patients with borderline tensions and no other findings of glaucoma after complete work-ups. Perhaps extended studies and observation of these borderline tension patients that will be discovered, some of whom will receive treatment and some of whom will not be treated but only observed, may teach us many things about the progress of visual loss in glaucoma in relation to the influence of treatment.

F. STERLING DAVIS, M.D., Washington, D. C.: [This discussion is published as a *Special Report* on page 142 of this issue.]

DR. PORTER: I wish to thank Dr. Kantar for his remarks, and I am happy that we have been able to present additional evidence of the diagnostic value of routine tonometry. I agree with his remarks about the necessity of the ophthalmologist bearing the responsibility for glaucoma detection. Although we do talk about interesting internists and general practitioners, I think we will still have to do most of the glaucoma detection for some time.

I should also like to commend Dr. Davis for exposing what he has charitably called an ineffective instrument. I am sure that if this instrument gets into the hands of the nonmedical eye people a great deal of harm can come to the detection and management of glaucoma.

INFLUENCE OF CIRCULATION ON EXTENT OF INVOLVEMENT AND TREATMENT IN EPITHELIOMAS OF THE UPPER RESPIRATORY AND DIGESTIVE TRACTS

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THE assumption that the growth and spread of epithelioma of the upper respiratory and digestive tracts is influenced by circulation in the tumor bed is based mainly on two considerations: (1) the nourishment required for the growth of epithelioma is supplied chiefly through arterial capillaries in the tumor bed; (2) extension and metastasis of this cancer occur primarily via lymphatic capillaries, so that its spread may be influenced by factors which determine the movement of lymph. Because the nourishment of epithelioma is supplied through the arterial capillaries in the tumor bed, epitheliomas arising in richly vascularized primary sites are likely to grow more aggressively than those in which the tumor bed is less vascularized. Increased vascular supply to the tissues requires greater drainage facilities; therefore, well vascularized tissues are usually provided with more numerous and larger venous and lymphatic capillaries than those with sparser arterial vascularization. In some of the richly vascularized areas, movement of the contents in lymphatic capillaries is expedited by the contraction of muscle around these capillaries. This increase in facilities for lymphatic capillary drainage raises the likelihood of local and of regional lymph node spread of epithelioma.

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The influence of the circulatory characteristics in the tumor bed which have been described in the preceding paragraph should be taken into account when attempting to form a clinical estimate of the extent of involvement and to plan the limits of the areas to be excised or irradiated. The possibility should be considered of placing the normally contracting muscles surrounding lymph capillaries at rest and of substituting, when this is practical, other ways to accomplish their function. If this is to be carried out, it should be done as soon as feasible, before metastases have reduced the possible usefulness of this substitution.

Other factors besides circulatory changes in the tumor bed influence the growth and spread of epithelioma of the upper respiratory and digestive tracts. Some growth tendencies inherent in individual types of epithelioma do not vary irrespective of circulatory changes in the tumor bed. The extent of involvement at the time the patient applies for treatment varies with such factors as the ease and accessibility of the cancer to clinical diagnosis, the cancer education of the patient and of the first doctor who examines the patient, the duration of the neoplasm before diagnosis. Nevertheless, it is felt that circulation in the tumor bed is one of the important influences affecting this problem. Consideration of this factor in deciding on the area to be excised or irradiated may improve the planning and, consequently, the results of treatment.

VASCULARIZATION AND GROWTH OF EPITHELIOMA

The reason for assuming that the degree of vascularization of the tumor bed may affect the natural history of epithelioma is that energy-releasing intermediate and essential metabolites needed for growth are delivered to the cancer directly or indirectly through the arterial capillaries in the tumor bed. Ribbert[27] emphasized the importance of blood supply for the growth of epithelioma by pointing out that necrosis of cancer occurs where the vascularization is inadequate, e.g., in the center of wide cancer strands, away from nourishing stroma. Ribbert believed that the original richness or scarcity of the normal arterial capillary network in the future cancer site plays an important role, even if the observation be true that there is a local increase in the number of arterial capillaries in response to tumor growth itself, as suggested by Goldmann,[11] and more recently by Algire and Merwin.[1]

Antopol, Glaubach and Graff,[2] working with mammary cancer 755 in C57 mice, noted a delay in the formation of new capillaries around tumor implants if, prior to the implantation, the mice received injections of cortisone. The tumor implants did not start to grow until the host's capillaries grew into them, though they remained viable by absorbing enough nourishment from their immediate surroundings. Similarly, Merwin, Algire and Kaplan[21] temporarily inhibited the formation of new capillaries around mammary tumor implants in mice by exposing the tumor bed prior to implantation to x-rays amounting to 3000 r in a single sitting. Growth of the tumor implants was delayed until the new capillaries coming from the host entered the cancer, presumably bringing needed nourishment for growth. According to Greene,[13] most tumor implants in the anterior chamber of the eye grow slowly for about three weeks, when they assume a pinkish appearance, i.e., become vascularized; after that, they grow much more aggressively. Lacassagne,[15] working with skin tar cancer in mice, was able to predict the site in which cancer would develop by finding vascularized patches when he examined the skin under a strong light.

Clinically, epitheliomas do not develop on the normally nonvascularized cornea, but they may start at the limbus, which is vascularized. According to Reese,[26] extensions of limbal epitheliomas onto the cornea are preceded by vascularization of the portion of the cornea which will be invaded.

The evidence presented above suggests that epithelioma does not grow in avascular tissues of the body and that before it will grow to a size which may be recognized clinically or microscopically, there occurs increased vascularization of the future cancer site.

Low oxygen content of the cell, according to Otto Warburg,[34] is one of the most important factors in the production of cancer. Graff,[12] on the other hand, looks upon this finding as the result and not the cause of growth. Authors disagree as to whether epithelioma develops more frequently in hyperemic or ischemic tissues. The frequency of papillomas and of epithelioma of the skin on the ears of tar painted mice was increased, according to Guldberg,[14] if he first produced a neuroparalytic hyperemia of the tumor site; this he did by extirpating the superior cervical ganglion and adjacent portion of the sympathetic nerve. Ritchie,[28] on the contrary, found an increase in the frequency of papillomas on the skin of rabbits' ears painted with 9-10 dimethyl 1-2 benzanthracene if, prior to the course of benzanthracene, these areas were made ischemic by partial occlusion of the carotid artery. Orr[23,24] also noted greater frequency of tar induced skin cancer in mice if the skin

was first rendered ischemic by one of two methods: either by temporary insertion of linen threads under the skin, which produced subcutaneous formation of scar tissue, or by subcutaneous injection of vascoconstrictor drugs such as Adrenalin.

Irrespective of whether cancer arises more frequently in a hyperemic or ischemic tumor bed, once established its further aggressiveness seems to be influenced by the adequacy of its blood supply: blood supplies oxygen, glycogen for energy, protein for synthesis and other substances needed for growth.

Some oxygen, according to Graff, is essential for growth of cancer; thus, because of deprivation of oxygen,[35] necrosis of cancer cells soon occurs in the center of a hanging drop tissue culture. When oxygen is completely excluded (and this is not easy to bring about),[36] mitosis seems to stop and growth to cease.[37] With low oxygen pressure continued for a long period, the cells die. Shorter periods cause irreversible tissue injury. Normal adult tissues die quickly under anaerobic conditions, yet they seem to do better under these conditions than cancer cells: thus, in tissue cultures, cancer cells grew only in the vicinity of the surface, accessible to oxygen, whereas normal cells often were able to grow throughout the culture medium.[12] Bierman, Kelly and Singer[5] compared the oxygen content of venous blood coming from cancer in twelve human patients with that of venous blood from other portions of the body in the same patients; the oxygen content in the veins coming from the cancer was higher and increased the nearer the cancer the samples were taken.

Energy for growth is furnished through the coupled processes of glycolysis and respiration, the first consisting in the nonoxidative degradation of glucose to pyruvic acid, the second yielding the bulk of the energy by completely oxidizing pyruvate. Caspersson and Santesson,[6] using ultraviolet microspectrophotometry to study metabolism of cancer cells, concluded that in spite of the tremendous increase of glycolysis in this disease, cancer cells in the center of wide tumor strands, away from the nourishing stroma, do not experience satisfaction of their glucose want; they found that fermentation is maximal in cells close to the region of arterial branching.

Protein synthesis is essential for growth of cancer, and according to Caspersson and Schultz,[7] a combination of protein and polynucleotides is characteristic of all self-reproducing systems. In an excellent study by roentgen absorption spectrophotometry of malignant transformation of squamous epithelium, Moberger[22] concluded that "significantly increased concentrations of nucleic acids were found in the cytoplasms of infiltrating cells in rapidly growing epidermoid carcinomas as compared with the homologous tissue of origin." Zamecnik and his colleagues,[40] on the basis of *in vivo* experiments on hepatomas in rats, concluded that "a small decrease in blood flow to a tissue might result in a large percentage decrease in protein synthesis." Caspersson and Santesson divided cancer cells into two varieties: (1) "A" cells which are rich in nucleotides, lying mostly at the periphery of cancer strands near the nourishing stroma or forming a mantle around capillaries, and (2) "B" cells, poor in nucleotides and lying in the center of cancer strands and not in proximity with nourishing stroma or blood capillaries. The "A" cells are the more actively proliferating, more aggressively growing cells; the "B" cells are the less active and less aggressively growing ones. In this connection, Ribbert's observation mentioned previously should be recalled, that necrosis starts mainly in the center

and not at the periphery of wide cancer strands. He relates the site of these necroses to inadequate vascularization. The possibility that the adequacy of vascularization may influence the growth of epithelioma in other ways, e.g., by the supply of growth stimulating hormones, has not been investigated in the present study.

The preceding experimental and laboratory evidence suggests that aggressively growing epitheliomas should be expected to occur more often in richly vascularized portions of the upper respiratory and digestive tracts rather than in the more poorly vascularized portions.

Clinically, invasive, rapidly extending, often undifferentiated epidermoid epitheliomas tend to predominate in such richly vascularized mucosae as those covering the soft palate, the aryepiglottic fold, the pyriform sinuses, and the pharynx. Exuberant, slowly progressing, often differentiated squamous cell epitheliomas are more common in the less vascularized mucosae of the hard palate, the maxillary antrum, and the anterior two thirds of the true vocal cord.

Inflammation tends to raise the blood supply of the tumor bed and is likely to increase the aggressiveness and extensiveness of epithelioma.

LOCAL EXTENSION AND LYMPHATIC METASTASIS OF EPITHELIOMA

Epidermoid epithelioma spreads primarily within lymphatic capillaries; evidently therefore lymphatic metastasis can not occur from or into tissues devoid of lymphatics. For instance, epithelioma invading the lymphatics of the conjunctiva does not involve the adjacent sclera, free from lymphatics. For the same reason, metastasis into the iris or ciliary body may grow next to but does not involve the crystalline lens. Other organs devoid of lymphatics are the epithelial covering of the skin and mucous membranes, the brain, parenchyma of the spleen, cartilage, and the placenta.[29,30] The absence of lymphatic metastasis does not preclude hematogenous metastases. Metastatic lesions of epidermoid epitheliomas of the upper respiratory and digestive tracts, on the whole, occur more rarely than in some other cancers and are seen mainly in the less differentiated types. Many of the patients with these epitheliomas either die, before the occurrence of distant metastases, from local extension of the primary growth, e.g., to an artery, from regional lymph node involvement, or are cured by treatment. The spread of epithelioma along the lymphatic system may be influenced by the anatomy and physiology of lymphatic capillaries and of regional lymph nodes and deserves careful consideration.

LYMPHATIC CAPILLARIES

The lymphatic capillaries form a system of endothelial tubes of varying caliber, suspended from a framework of connective tissue. This framework varies in different portions of the upper respiratory and digestive tracts depending on the number and caliber of the lymph capillaries and the direction and density of the meshes composing the local lymphatic plexus. These structural variations are influenced by drainage requirements of the individual location and correspond to the degree of arterial capillary development. Thus, the lymphatic plexus is usually dense, and narrow-meshed with large calibered, multilayered capillaries in regions which are well vascularized, e.g., in the mucosa supported by the loose areolar tissue of the soft palate, the pharynx, the posterior portion of the aryepiglottic fold, and the pyriform sinus. The lymphatic network tends to be sparse and widely meshed, and to consist of a single layer of narrow lymph capillaries in less vascularized areas where the connective tissue

TABLE I

DIAMETER OF LYMPHATIC CAPILLARIES IN MILLIMETERS

LOCATION	SUPERFICIAL (MM.)	DEEP (MM.)	SOURCE
Vocal cord	0.018		Teichmann
Aryepiglottic fold, posterior half	0.04	0.4	Teichmann
Tongue	0.018-0.027 (mucosa)	0.054-0.72 (submucosa)	Teichmann
Esophagus	0.02-0.07		Teichmann
Skin	0.018-0.054	0.094-0.144	Teichmann
Skin, scalp	0.039-0.04	0.115-0.150	Lavrientiev
Skin, cheek	0.02-0.06	0.06-0.08	Ignashkin
Skin, neck (adult)	0.06-0.1	0.08-0.15	Kurbskaja
Skin, neck (child)	0.015-0.05	0.05-0.08	Kurbskaja

stroma is dense and firm, e.g., in the mucosae of the hard palate, of the maxillary antrum, of the free edge of the anterior two thirds of the vocal cord, and of a vertical central strip on the laryngeal surface of the epiglottis.

A report on the diameters of injected lymphatic capillaries in cadavers was published by Teichmann[33] in 1861, and a more recent report was prepared by Schdanov and his associates.[29,30] A few of these measurements are given in table I.

The larger diameter of deep lymphatic capillaries, as compared to those which are superficial, partially explains the greater frequency of regional lymph node metastases in advancing clinical stages of epithelioma, e.g., in those of the tongue. It is logical to assume that more epithelioma cells will enter lymphatic capillaries having a diameter of 0.054 to 0.72 mm. than capillaries having a diameter of 0.018 to 0.027 mm. In stage I only the latter narrower mucosal lymphatics are involved; in stages II, III and IV the wider submucosal lymph capillaries are involved in the process.

In addition to the caliber of the lymphatics, other factors in the tumor bed affect the movement of lymph and, therefore, the spread of epithelioma. Movement of the contents in lymphatic capillaries differs from that in arterial capillaries. According to Starling,[31] blood in arterial capillaries is moved rapidly at a relatively high intraluminal pressure, aided by the semirigidity of the elastic muscular walls of the arterial system. This pressure is reduced by the increase in total volume of the arterial tree as one progresses from the aorta toward the capillaries: the average diameter of the aorta is believed to be somewhere near 3 cm., and the total volume of arterial capillaries is said to be 800 times greater. It is not surprising, therefore, that the intraluminal pressure falls correspondingly as follows: the mean pressure in 1 cm. of water in the larger arteries is 135 cm.; it is 90 cm. in the arterioles, and 35 cm. in the arterial capillaries. In the venous capillaries it is 30 cm., in venules 15 cm., and in the subclavian vein it is from 4 to 6 cm. The latter is lower than the pressure within the thoracic duct, which is from 6 to 10 cm.; this relationship facilitates the flow of lymph into the subclavian vein.[29,30]

Lymph in peripheral lymphatic capillaries moves sluggishly; it is not pro-

pelled by contraction of the left ventricle. The walls of lymphatic capillaries are devoid of muscle; they are lax and the intraluminal pressure in them is near zero. Primitive lymphatic capillaries consist of only a single layer of endothelial cells, perhaps surrounded by a few connective tissue fibers; these develop into a definite adventitia as one progresses centripetally and the lymphatic capillaries assume a larger diameter. With further increase in the caliber, smooth muscle fibers appear in the wall; in a number of them, especially in the thoracic duct, there is a true muscle coat. The contraction of these smooth muscle fibers tends to shorten the lymphatic vessel, and this may help in the movement of lymph. However, according to Drinker and Yoffey,[9] other more important factors also affect the flow of lymph.

Movement of lymph depends primarily on three forces outside of the lymphatic system:

1. The plasma leaks from arterial capillaries into tissues surrounding the lymphatic capillaries. This raises the hydrostatic pressure around the lymphatic capillary, which, according to the beautifully illustrated conception of Young and Griffith,[39] facilitates the entrance of the fluid surrounding the capillary into its lumen. This in turn increases the intraluminal pressure and furnishes more lymph for the transportation of epithelioma cells; therefore, the richer the vascularization of the tumor bed, the more plasma will enter the local lymphatic capillaries, the greater will be the flow of lymph, and the more likely is the spread of the epithelioma.

2. Contraction of muscle surrounding the lymphatic capillaries; such muscle is well developed in some sites and is less marked in other portions of the upper respiratory and digestive tracts. Where present, its contraction propels lymph and other contents of lymphatic capillaries in a centripetal direction, toward the thoracic and right lymphatic ducts, and increases the intraluminal pressure. The importance of this rise in intraluminal pressure for the movement of lymph (and epithelioma cells) in lymphatic capillaries may be appreciated from the following experiment by Drinker and Field.[9] These authors inserted a cannula into a lymph collecting tubule in the leg of an anesthetized dog. When the leg was at rest, lymph did not flow out of the cannula; only when the leg was moved or massaged, and the pressure within the lymphatic thus raised, did the lymph flow out of the cannula. This observation suggests that movement in peripheral lymphatic capillaries may be expedited in locations in which contraction of muscle surrounding the capillaries squeezes the contents centripetally; examples of such locations are the soft palate, the tongue, the pharynx, and the esophagus. Movement of the contents in lymphatic capillaries is likely to be more sluggish where contracting muscle does not play an important role, e.g., the mucosa covering the hard palate and maxillary antrum or the free edge of the vocal cord. Local extensions and regional lymph node involvement should, therefore, be more frequent and more extensive in epitheliomas growing in tumor beds in which muscle surrounds the lymphatic capillaries than in those in which it does not. In this connection an observation of Pullinger and Florey[25] is interesting, namely, that lymph capillaries are "intimately connected to the surrounding tissues by collagen and reticulum fibers." Contraction of muscles surrounding lymph capillaries not only helps to move the contents of the capillary centripetally, but by pulling on the wall, the contraction may also open spaces between the cells of the endothelial lining and thus facilitate the en-

trance into the capillary lumen of bacteria and cells, including, one would suppose, cancer cells.

3. Finally, movement of lymph is influenced by contraction of costal muscles and diaphragm in breathing; this propels and sucks lymph alternately from and into the thoracic and abdominal cavities.

The relative importance of the above three forces in the movement of the contents of lymphatic capillaries varies in different locations in the body. The first two affect, primarily, movement in the peripheral lymphatics, and the third probably influences especially the flow of lymph in the peritoneum, pleura, and abdominothoracic organs.

The maintenance of the centripetal direction of flow within lymphatic capillaries is aided by valves. These are folds of intimal lining facing in the direction of the current which prevent the reflux of lymph once it has passed the site of the valve. Lymph is thus kept constantly moving toward the thoracic or the right lymphatic duct and cannot flow in the opposite direction under normal conditions. The valves are placed at frequent intervals in the peripheral lymphatics and become rarer as one approaches the region of the thoracic duct. Because of the low intraluminal pressure in the lymph capillaries, insufficiency of the valves may result in retrograde flow if there is enough obstruction to the centripetal direction of the current, e.g., by a proximally placed mass of inflammatory or neoplastic tissue. Often these obstructions start in the region of a lymph node which has been filled by growth of epithelioma cells.

REGIONAL LYMPH NODES

Regional lymph nodes are usually the first site of metastasis in epithelioma, and their anatomic location has been the subject of numerous studies. Information as to their normal location in relation to the individual cancer sites is essential for correct planning of the treatment areas for excision or radiotherapy. This information is outside the range of the present study and will not be discussed here. It would appear, however, that the frequency of regional lymph node involvement is usually greater where the tumor bed is rich in arterial and lymphatic capillaries, especially where the latter are compressed by surrounding muscle, than where these three circulatory aids do not exist. Mascagni[18] believed that small lymphatic vessels never enter directly into large ones, but always first pass through a lymph node. Schdanov[29,30] believes that there are some exceptions to this rule. The lymph particles and cells floating therein enter through afferent lymphatics into the marginal sinus at the periphery of the node and either progress directly to the efferent vessel or through the intermediate sinuses in the cortex and medulla, then leave the lymph node through the efferent vessels at the hilum. Circulation in the lymph node is described by Yoffey and Courtice[38] as follows:

> Lymph flowing in through a number of narrow channels and under a very definite head of pressure finds itself in a huge space with an enormous number of rich and irregular paths leading to the hilum vessel. The flow is instantly slowed and the driving head of pressure practically lost. Not only are the sinuses in the node a perfect settling chamber, but the reticulum which they contain furnishes a multitude of baffles, which again slow down the lymph flow and make it easy for the phagocytic cells composing the reticulum to perform their function.

The sinuses of the regional nodes are, therefore, an ideal site for epithelioma cells to settle without being floated away by the current of lymph. Clumps of these cells can attach themselves to the intima lining the sinus walls, become vascularized, thus getting better nour-

ishment, and finally start growing as a full fledged metastatic growth. This growth may eventually fill and destroy the lymph node. From a clinical standpoint it is important to remember that the filtering action of lymph nodes is reduced by massage. Thus vigorous palpation, even the normal movements of the head which compress neck structures, as well as contraction of the muscles in swallowing, may increase passage of cancer cells through an invaded lymph node.

A review of everything that has been said in the preceding pages permits the assumption that epitheliomas of the upper respiratory and digestive tracts are likely to grow more aggressively, metastasize earlier and, consequently, be more extensive when the patient applies for treatment if the following circulatory conditions prevail in the tumor bed: rich vascularization, rich lymphatic drainage, and muscle compressing the lymphatic capillaries. Epitheliomas growing in tumor beds with scant vascularization and lymphatic drainage and no muscle surrounding the lymphatic capillaries are likely to grow slowly, show late local extension and regional lymph node metastasis and limited extent of involvement at the time the patient applies for treatment. Examples of the first group of tumor beds are to be found in epitheliomas arising in the region of the base of the tongue,[32] the faucial tonsil,[10] the soft palate,[37] and the pharynx.[32] Most of these epitheliomas tend to grow rapidly and invasively and to metastasize to regional lymph nodes in close to 60 per cent of the cases. Epitheliomas originating in and still limited to primary sites in regions of the hard palate,[32] the maxillary antrum,[32] and the free edge of the anterior two thirds of the vocal cord represent growths in tumor beds of the second group. These are poorly nourished and less efficiently drained, and no muscle surrounds the lymph capillaries; therefore, they tend to grow more exuberantly, spread slowly, and metastasize late, e.g., there are practically no regional node metastases in epitheliomas limited to the free edge of the anterior two thirds of the vocal cord. Here there is only a single layer of lymph capillaries; their diameter averages 0.018 mm. and Reinke's space and the nucleus elasticus separate the subepithelial lymph capillaries from the thyroarytenoideus muscles. Metastasis to the cervical lymph nodes occurs in about 30 per cent of epitheliomas of the anterior portion of the laryngeal vestibule, according to Baclesse,[3] and in 70 per cent of those of the posterior part. Lymph drainage of the anterior portion consists of a single layer of lymphatic capillaries averaging 0.03 mm. in diameter and muscular contraction here is much less than in the posterior portion. Posteriorly there is a double layer of lymph capillaries, the superficial one having a diameter of 0.04 mm., and the deep one, 0.4 mm. The difference in the proportion of lymph node metastases, therefore, may be explained by the variations in drainage facilities. On the basis of much experience, Clerf[8] feels that prophylactic neck dissection is indicated in all cordal cancers with extension to the subglottic region or arytenoids, and in all primary epitheliomas of the supraglottic and infraglottic areas; lymphatic drainage in these regions is much richer than on the vocal cord.

The above differences in circulation of the tumor bed indicate treatment fields which go wide of the clinically appreciable local limits of the epithelioma and routine treatment of regional lymph node areas, whether clinically involved or not, in epitheliomas growing in tumor beds of the first group. On the other hand, in cancers of the second group it may suffice to treat narrow margins around the local clinical limit of the cancer, without prophylactic neck dissec-

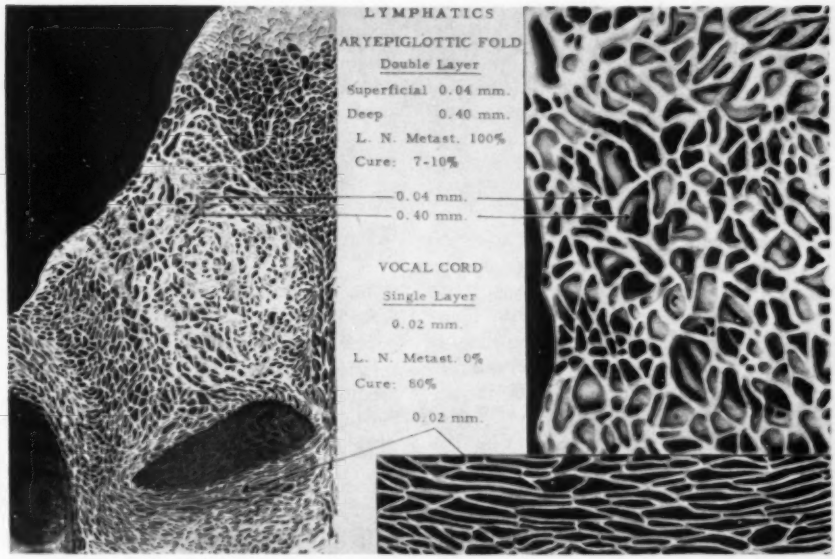

FIG. 1—In addition to the smaller number and caliber of lymphatics in the vocal cord, these are separated from the vocal muscle by elastic tissue; muscle is close to lymphatics in the aryepiglottic fold.

tion or prophylactic radiotherapy to regional nodes. For example, simple cordectomy or narrow field radiotherapy is likely to cure most epitheliomas limited to the free edge of the anterior two thirds of the vocal cord; yet, even radical laryngectomy or wide field radiotherapy or both, including prophylactic neck dissection or prophylactic radiotherapy to the neck, often fails to cure epitheliomas of the lower portion of the pyriform sinus.

In view of the role played by muscle contraction around lymphatic capillaries, it would seem logical to consider reduction of the need for this contraction by substituting other methods of accomplishing the function of these muscles. It is advantageous to do this early, before metastasis has reduced the possible usefulness of this procedure. For instance, in epithelioma of the mucosa of the cheek, the need for contraction of the masseter muscles may be reduced by placing the patient on a liquid diet as soon as the diagnosis has been made; in epithelioma of the soft palate, the posterior portion of the tongue, the aryepiglottic fold, the pyriform sinuses, the pharynx and the cervical esophagus, tube feeding or gastrostomy will diminish the need for contraction of the muscles concerned with swallowing. Though logical, this suggestion should be applied only with the realization that it still requires the support of extensive clinical experience.

Circulation in the tumor bed, of course, does not represent the only factor determining the growth and extension of epithelioma of the upper respiratory and digestive tracts; many other influences also affect this problem. Thus, inherent growth tendencies characteristic of individual growths or of types of epithelioma may persist irrespective of circulatory changes in the tumor bed. Taylor and Nathanson,[32] for instance, noted an increase in the proportion of metastatic lesions in the lymph nodes from

6 per cent to 30 per cent to 52 per cent as the microscopic grading rose from I to II to III in 579 epitheliomas of the lower lip. In 126 patients with epithelioma of the buccal mucosa, grade I, the proportion of metastatic lesions in the lymph nodes was 24 per cent; it was 45 per cent in 93 patients with microscopic grade II and grade III. In other words, the frequency of lymph node metastasis was greater in the less differentiated epitheliomas of the oral mucosa irrespective of the primary site of the growth. These natural growth characteristics influence the extent of involvement which the cancer is likely to reach by the time the patient applies for treatment.

Many other factors also affect the extent of involvement at the time of treatment; among these should be mentioned the ease and accessibility of the cancer to clinical diagnosis. For instance, epithelioma of the lower lip in patients seen at the Curie Foundation in Paris was diagnosed by Baud[4] in stage I in 43 per cent of 287 applicants for treatment, whereas only 5 per cent of patients applied after their cancer had reached stage IV. On the other hand, in epithelioma of the mucosa of the cheek,[16] which is much more hidden, the respective proportions were for Stage I, 11 per cent of 131 patients, and for Stage IV, 21 per cent.

Another factor is the cancer education of the patient and the first doctor who examines the patient. Good cancer propaganda tends to bring patients with easily recognizable cancers to the doctor in earlier stages than when no effort has been made to educate either the public or the medical profession. Good cancer propaganda is exemplified by the work of the American Cancer Society.

The duration of the neoplasm before diagnosis, of course, must have an influence on the size of the cancer at the time when the patient applied for treatment. This is shown by the advanced clinical stage of the epithelioma when the patient seeks medical advice — the longer the disease has existed, the more advanced, usually, is the stage of the epithelioma.

In spite of the various factors just discussed, it is felt that circulation in the tumor bed also influences the growth and extent of epitheliomas of the upper respiratory and digestive tracts.

In their book on metastasis to the lymph nodes, Taylor and Nathanson[32] correctly suspected that there may be a relationship between the variation in the frequency of these metastatic lesions, depending on a difference in the caliber of lymphatics, and movement in the various sites of intra-oral epithelioma.

In a personal communication, McWhirter[20] independently suggested movement as a major force in producing metastasis to the lymph nodes in intraoral cancer sites. Masson[19] related the paucity of metastatic growths from carcinoids of the appendix and their frequency from carcinoids of the small intestine to more forceful peristalsis in the intestine. However, it was the anatomic studies of the diameter of lymphatics,[17,29,30,33] and the physiological investigations of the movement of blood and lymph[9,25,31,38,39] correlated with personal clinical experience and that of others which helped to explain differences in growth behavior of epitheliomas in various locations of the upper respiratory and digestive tracts.

Some of the conclusions reached in the preceding pages may have to be modified. We believe, however, that the theory will be upheld that the circulation in the tumor bed influences the growth and extension of epithelioma. Consideration of this factor in deciding on the areas to be excised or irradiated may improve the planning and, therefore, the results of treatment of these cancers. As contraction of muscle around

lymphatic capillaries may increase the spread of epithelioma, the suggestion seems logical that this threat may be reduced by substituting other means to accomplish its function and thus place the muscle at rest. It is realized, however, that the practical application of this expedient may at times have to be modified and that the method may not be indicated in some instances. The whole subject of the relation of circulation in the tumor bed and growth of epithelioma is one of practical interest to those working in cancer research and deserves further study.

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DISCUSSION

JOHN F. DALY, M.D., New York: Tumors show great variations in their clinical behavior, but among these variations certain patterns can be discerned. One of these is that the incidence of metastasis tends to vary according to the anatomical site of the tumor. To find an explanation for this, Dr. Lenz has restudied the tumor bed and has found a definite correlation between the incidence of metastasis and (1) the vascularity of the area, (2) the size and development of the lymphatic vessels, and (3) the motility of the area. He has amply supported his thesis with both experimental and clinical evidence.

He has made this his main theme and presented it in the major key in order that its full implications may be seen. At the same time, he points out that other factors influence the behavior of the tumor; namely, its inherent biological tendencies. Tumors are like human beings, they have traits which cannot be attributed to their environment and can be explained only on the basis of their chromasomes. Epitheliomas arising in the same anatomical area may show wide variations in their ability to grow, invade and metastasize.

Thus the clinical behavior of any epithelioma will be the resultant of these two factors: (1) the intrinsic character of the tumor and (2) the environment offered by the tumor bed.

Dr. Lenz has added a new dimension to this dynamic picture of the tumor field by stressing the role of muscle action in moving fluid from the tissue spaces into and through the lymphatic vessels. That muscle action could be responsible for variation in rates of metastasis has not been presented so clearly before.

As a practical application of the importance of muscular action in dissemination of cancer cells, Dr. Lenz suggests that the part involved be put at rest. This will be a more formidable problem for the radiotherapist, who must treat his patient over a four-to-six-week period. For the surgeon it raises the question of how much his manipulation of the tumor bed before and during the operation may be responsible for dissemination of tumor cells. For example, in considering aspiration for a biopsy of a cervical node in the field of drainage of a proved primary lesion, the surgeon should ask himself whether the information gained is important enough to outweigh the definite risk of spread of disease. This concept of the tumor bed should be used in analyzing every tumor problem.

By stressing the role of muscular action in dissemination of tumor cells, Dr. Lenz has made an important contribution to our understanding of tumor behavior.

THE COMPREHENSIVE SURGICAL TREATMENT OF NASAL POLYPOSIS

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THE difficulties and disappointments attending the treatment of nasal polyposis have been experienced by every rhinologist. The tendency for recurrence of polypi is too well known to need emphasis. No single method or combination of methods of treatment has yet been devised which can be depended on to bring permanent relief to all patients. In Mayo Clinic experience, however, comprehensive surgical treatment has brought patients with nasal polyposis the greatest degree of relief for the longest time.

PATHOLOGY

The pathogenesis of nasal polypi is not fully agreed on by writers on the subject. Allergy and infection are generally accepted as the principal causes of polyposis, emphasis being placed on one or the other according to the major interest of the author.

Hansel[3] reported finding polyps in 25 per cent of unselected cases of nasal allergy and mentioned Kern and Schenck's report of nasal polypi in 30 per cent of patients suffering from asthma. Kern and Schenck had written also that polypi are seldom encountered in patients with suppurative sinusitis associated with pulmonary lesions.

Eggston and Wolff[2] stated:

> The common polyp represents an edema and simple hypertrophy of the nasal mucosa resulting from an inflammatory process. Unless the infection is removed, the polyps will continue to appear, even though they are superficially removed. In order to discontinue the process of polypoid formation, it is necessary to remove the infectious process. This is not always so easily accomplished in so complicated a structure as the nasal sinuses.

The same authors gave the opinion that polyps arise because of basic vascular changes in the nasal mucosa which are induced by chronic and repeated attacks of sinusitis. The infection causes periphlebitis and perilymphangitis; then these impede the return of interstitial fluids, as the obstruction affects the veins, the artery remaining intact. Fluids enter but do not leave. This results in distention of tissues and reduced oxidation, eventuating in edema.

Taillens[4] offered the view that polypi are the result of a combination of infection and allergy. He stated that polypi arise first within the sinuses—primarily the maxillary sinus—later extending into the nasal chamber, and that the infection from which they proceed is a natural consequence of impaired drainage within the sinuses secondary to allergic edema of the mucosa. The allergy is atypical, failing to respond to desensitization measures. Tissue eosinophilia is not a constant finding and of itself has little clinical significance, but eosinophilia of more than 10 per cent in the blood is a bad prognostic sign for polyposis.

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Taillens considered the maxillary sinus the most frequent point of origin of nasal polypi. This is logical, since lack of dependent drainage makes the maxillary the most vulnerable of all sinuses to chronic infection. In our experience, however, manifest polyposis has the ethmoid labyrinth as its most frequent and earliest site. Polypi are found in the maxillary sinus in most cases of severe polyposis, but they appear less frequently in the sphenoid and frontal sinuses.

Nasal polyposis is reversible only in its early stages. Newly formed polypi observed during the edematous phase of acute rhinitis or of acute nasal allergy can be resorbed when the source of irritation is eliminated. Older polypi which show changes in the walls of their blood vessels resulting in vascular insufficiency are capable of permanent remission, spontaneous or induced, in only a few cases.

MATERIAL AND METHODS

Selection of Cases

The records of patients who underwent surgical treatment for nasal polyposis with concomitant sinusitis in hospitals associated with the Mayo Clinic during the years 1949, 1950, and 1951 were reviewed. Instances of antrochoanal polyps and cases not seen at least one year after operation by a rhinologist of our group were not included. Found qualified for study were a total of 120 cases with follow-ups ranging to seven years.

Techniques

The records used represent the work of a group of surgeons who, while subscribing to the same general principles, nevertheless interposed their personal variations in judgment and technique. Our general policy has been to individualize the treatment, applying the surgical measures deemed indicated by preoperative findings in each case rather than doing a prescribed operation in all cases. This results in more extensive operation in those cases which present greater degrees of polyposis and infection.

All of the operations were accomplished by the intranasal approach. If preoperative examination had disclosed morbidity in the antrums, grossly diseased mucosa was removed insofar as was possible, the grossly normal tissue being preserved. If morbidity had been discovered in the ethmoid sinuses, visible mucosa was removed carefully from them by curet. The sphenoid sinuses were investigated at operation, and when disease was demonstrated they were opened and stripped of mucosa. As a rule, the frontal sinus was not disturbed. This technique did not provide for stripping all mucosa from the maxillary sinus, from the floor of the ethmoid labyrinth, or from orbitoethmoid and frontoethmoid cells when these were present. Submucous resection of the nasal septum was performed when indicated but has not been considered in evaluation of the results.

It has been our practice to use intranasal irradiation as an adjunct to surgical measures in cases of severe polyposis and cases in which prior surgical treatment has been followed by rapid recurrence. This process of selection makes comparison with the general group difficult.

Two or four capsules, each containing 50 mg. of radium encased in 1.5 mm. of brass, were applied to the sphenoethmoid and maxillary areas at the completion of the operation and were removed at the end of three hours. The brass screen absorbed the beta rays but allowed the gamma rays to enter the tissues. The dose was 150 mg. hours from each capsule.

Antibiotic therapy was used post-

operatively for two to five days in all cases. Steroid therapy was used so seldom that it is not a factor in the results. The study, then, is basically a comparison of the effectiveness of surgical procedures of various extent.

Classification of Operations

Conservative surgical treatment—the removal of a few nasal polypi as they recur from time to time—was ruled out of the present study with the exclusion of that kind of case. The operations performed in this series are all of relatively extensive scope, although the variation among them is rather wide, as determined by the conditions found. In classifying these procedures for comparison of results achieved, consideration has been focused principally on the latest operation in the history. The scheme of classification follows: (1) comprehensive, either (a) primary or (b) secondary; and (2) limited, whether (a) progressive, (b) primary, or (c) secondary.

Simply stated, a *comprehensive* procedure was one in which the polypi were removed from both the nose and the paranasal sinuses, with provision for free drainage of products of infection from the sinuses, and as much mucosa as possible—both polypoid and potentially polypoid—was removed from the maxillary sinus and ethmoid labyrinth, and from the sphenoid and frontal sinuses when necessary. The frontonasal duct was exposed during ethmoidectomy in most instances. Turbinate tissue was preserved to the greatest degree practicable.

Limited procedures exceeded the conservative measures mentioned by including treatment of either the maxillary or the ethmoid sinuses. Actually, *progressive* signifies a completed series of operations which amounted to comprehensive treatment; but inasmuch as the successive stages were employed to meet successive conditions—recurrences of polypi—rather than as parts of a concerted plan, and the latest stage was in itself a limited operation, it is classed with that general type. The other limited procedures differed from the comprehensive in that, because evidence of polyposis or infection was not found therein at preoperative examination, either the antrums were not opened or the ethmoid labyrinth was not exenterated.

FINDINGS

Classification of Follow-up Observations

All of the 120 cases were classified in accord with the findings at the latest observation by a rhinologist of our group.

1. *No recurrence* signifies that no recurrence of polypi was seen at observation at least one year after operation; all cases in which recurrence was found at any time after operation are reported as recurrent.

2. *Asymptomatic recurrence* signifies that the polypoid hyperplasia and small polypi found did not extend below the level of the inferior margin of the middle turbinate and that further surgical treatment was not advised at the time of observation. Asymptomatic polypi may enlarge, however, to become symptomatic.

3. *Symptomatic recurrence* signifies that the polyposis observed was greater than that described for category 2.

Consideration of Results

The results of all operations and a comparison of results from those classed as comprehensive and those classed as limited are presented in table I. No recurrence was observed in 47 per cent of all cases; but on further classification no recurrence was found in 62 per cent of cases in which comprehensive operation had been performed, as compared to 34

TABLE I

RESULTS OF ALL OPERATIONS

RECURRENCES	OPERATIONS				TOTALS	
	COMPREHENSIVE		LIMITED			
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
None	34	62	22	34	56	47
Asymptomatic	10	18	20	31	30	25
Symptomatic	11	20	23	35	34	28

TABLE II

RESULTS OF LIMITED OPERATIONS CLASSIFIED BY EXTENT

RECURRENCES	OPERATIONS						TOTALS	
	PROGRESSIVE		NOT ANTRUMS		NOT ETHMOIDS			
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
None	2	20	16	34	4	50	22	34
Asymptomatic	4	40	16	34	0	0	20	31
Symptomatic	4	40	15	32	4	50	23	35

TABLE III

RESULTS OF COMPREHENSIVE OPERATIONS CLASSIFIED BY PRIORITY

RECURRENCES	OPERATIONS				TOTALS	
	PRIMARY		SECONDARY			
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
None	17	74	17	53	34	62
Asymptomatic	3	13	7	22	10	18
Symptomatic	3	13	8	25	11	20

TABLE IV

RESULTS OF LIMITED OPERATIONS CLASSIFIED BY PRIORITY

RECURRENCES	OPERATIONS				TOTALS	
	PRIMARY		SECONDARY*			
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
None	13	43	9	26	22	34
Asymptomatic	6	20	14	40	20	31
Symptomatic	11	37	12	34	23	35

*Including progressive.

TABLE V

RESULTS WITH RADIUM THERAPY AS ADJUNCT TO OPERATION (32 CASES)

RECURRENCES	OPERATIONS							
	COMPREHENSIVE				LIMITED			
	PRIMARY		SECONDARY		PRIMARY		SECONDARY	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
None	2	67	6	60	2	40	6	43
Asymptomatic	1	33	1	10	1	20	6	43
Symptomatic	0	0	3	30	2	40	2	14

per cent of cases in which limited measures were applied. After the operations of each type, the asymptomatic recurrences were approximately equal in number to the symptomatic.

Among limited operations, including the progressive, table II distinguishes whether it was the antrums or the ethmoid sinuses which were not treated surgically. The rate of recurrence is approximately equal in all groups, variations from the mean occurring in the smaller groups. This table suggests that the ethmoid and maxillary sinuses are equally important as sites of recurrence. When recurrence was observed, polyposis often was seen also in the sinuses not previously treated surgically.

Cases of comprehensive operation and limited operation are divided in tables III and IV into those in which the reported procedure was the primary or secondary operation done for polyposis. It is apparent that in both classes the results have been more favorable when the operation was accomplished in a field not previously subjected to surgical treatment. Scar tissue and sclerosis of bone resulting from previous surgical intervention increase the difficulty of dissection and consequently decrease the possibility of adequate removal of diseased mucosa.

The results observed after operation and radium therapy in 32 cases are summarized in table V. These very small subgroups of cases reported do not amount to conclusive evidence, but the findings closely approximate those from the total group of cases, except for the instances in which a secondary limited operation was employed. Within this subgroup, results in those cases in which radium was used were better than those in the entire group. It should be repeated that the cases selected for radium therapy were the most difficult ones.

COMMENT

Comprehensive surgical treatment is not recommended in all cases of nasal polyposis. Acute polyposis arising in the course of acute allergic or inflammatory rhinitis often resolves spontaneously as the rhinitis subsides, and nonsurgical treatment usually is effective in such cases. Also, solitary polypi do not justify so extensive a surgical procedure, particularly if the point of origin is within the nasal cavity; often conservative removal of such polypi is followed by relief of several years' duration. Comprehensive surgical treatment is recommended for cases in which multiple polypi arise from the ethmoid and maxillary sinuses.

The observations reported in this study indicate a definite correlation between extent of the surgical procedure and incidence of recurrence of nasal

polypi. The more extensive procedures resulted in significantly lower incidence of recurrence. Further evidence in this direction is elicited by comparison of our results with those presented by Diamant and Ottosson.[1] These authors have reported on a series of patients treated by external radical maxillary sinusotomy and transantral ethmosphenoidostomy, with removal of all antral mucosa in each case. In dealing with the ethmoid sinuses, this operation removes the floor and its attached mucosa. Thus it is more extensive than the intranasal operation reported in our series. Results of the two series are shown in table VI. I believe that improved results reported by Diamant and Ottosson stem from more comprehensive removal of sinal mucosa.

TABLE VI

RESULTS OF COMPREHENSIVE INTRANASAL AND TRANSANTRAL OPERATIONS

RECURRENCES	INTRANASAL* MAYO CLINIC	TRANSANTRAL DIAMANT-OTTOSSON
None	62%	80.3%
Asymptomatic	18%	9.4%
Symptomatic	20%	10.3%

*Inasmuch as the transantral series included both primary and secondary operations, this group also contains both categories for the comparison.

Comprehensive surgical treatment achieves its highest degree of success when employed as the primary surgical procedure. This is evident not only in the percentage of nonrecurrence but, just as importantly, in the preservation of nasal function. Removal of polypi is, in a sense, removal of nasal mucosa. Repeated partial polypectomy results in a much higher incidence of surgical atrophy than does a single operation of sufficient scope to cure the disease.

In its pathologic aspect nasal polyposis is, according to Eggston and Wolff, a progressive process. Certainly progressive atrophy of the nasal mucosa and loss of the sense of smell result from the persistent and increasing pressure of nasal polypi, and the preservation of a physiologically adequate nasal mucosa is greatly favored by early operation. The surgeon must possess great courage to advise an extensive surgical procedure at an early stage of polyposis, but I am convinced that comprehensive operation done as a primary procedure in the early stages of polyposis offers the greatest advantages both in rate of cure and in preservation of nasal function.

The results achieved by the addition of radium therapy in recurrent cases indicate to me that this is a valuable adjunct to the secondary limited surgical operations employed in such a situation, and suggest a possible usefulness in other severe cases.

SUMMARY AND CONCLUSIONS

Study of 120 cases of nasal polyposis treated at the Mayo Clinic by intranasal operation on polypi and sinuses shows an over-all rate of nonrecurrence of 47 per cent one to seven years after operation. Nonrecurrence was noted in 62 per cent of cases in which all sinuses were operated on, and in 34 per cent of cases in which operation on some sinuses was omitted because they were considered free of disease at the time of operation. Nonrecurrence was observed in 74 per

cent of those cases in which all sinuses were operated on at the initial operation for polyposis.

In selected cases of severe disease, intranasal irradiation with radium was employed in conjunction with the operation. Generally, the incidence of nonrecurrence approximated that of cases not treated by irradiation.

Nonrecurrence of polyps was reported by Diamant and Ottosson in 80 per cent of cases treated by external antrostomy and transantral ethmosphenoidostomy.

From this study the following conclusions seem warranted.

1. Nasal polyposis may be effectively treated by surgical means.

2. A comprehensive operation to remove polyps and potential polyp-bearing mucosa from the nose and sinuses produces better results than more conservative surgical measures.

3. The best results, particularly with regard to preservation of nasal function, are obtained when the comprehensive procedure is the first operation employed.

4. Radium therapy is a useful adjunct to surgical measures in some circumstances, but it is less important than adequate operation.

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DISCUSSION

FRANCIS L. LEDERER, M.D., Chicago: Many facets of the nasal polyp problem are posed by Dr. Simonton's excellent presentation. It does, however, offer numerous opportunities for challenge in the light of past literature and personal experiences. The greatest figure of Arabic medicine, Avicenna (970 to 1037 A.D.), who wrote the *Canon of Medicine*, likened polyps to hemorrhoids and advised their ligation. Hippocrates, who could well be designated as the Father of Rhinology, described five kinds of polyps and gave a snare technique for their removal around 460 B.C. In 1698 St. Hilaire stated, "When heat and disturbance enter the blood, its viscosity increases and the viscid parts are extruded. The heat fixes and condenses them and when abundant in a spongy structure, as the nose, furnishes the substance for polyps that swell the vessels and dilate the glands." Over two centuries ago Morgagni described polyps as originating more in the nose than in the sinuses. The controversy of the past continues to appear in the literature with such names as Billroth, Hopmann, Zuckerkandl, Hajek, Uffenorde, Killian, Kubo, Hirsch, Semenov, Van Alyea, and many others; now Simonton, venturing thoughts on the pros and cons of the site of origin, joins the therapeutic free-for-all.

From evidence which is available we cannot view nasal polyps as a purely local disease which responds readily to antiallergic, antibacterial therapy or to a surgical approach with a snare or a curet. In almost nine and one-quarter centuries of trial and error, the mechanical removal of polyps, although falling far short of its goal, is still the most popular rhinologic procedure.

Dr. Simonton referred to J. P. Taillens, who feels that nasal polyposis is not an entity but a symptom. He speaks of an allergic terrain and expresses the thought that "pure" allergy does not seem to generate polyps. Most often these patients are more complex, even parallergic, i.e., sensitive to weather changes, food, dust, and medications. If we accept these observations, we can better understand the failure of specific desensitization, the partial success of antihistamines, and the transient effect of steroid therapy. Taillens noted that in bronchial asthma, a frequent complication of polypoid sinusitis, a true allergic asthma

was rare, but asthmatiform bronchitis was common. It was in the latter that an aggresive surgical attack, referred to as "comprehensive" by Dr. Simonton, seemed to be effective or, at least, to bring about pronounced amelioration. Taillens did not find this to be the case in instances of true allergic asthma which not only did not improve but even worsened after the operation.

Rather than accept the thesis that failure to eradicate polyps is due solely to improper allergic management or to inadequate surgical exenteration of sinus cavities, I have, in association with Dr. Max Samter of the University of Illinois, decided that the basic difference rests on who it is who has the polyps. Patients are classified into two separate groups: viz., (1) the larger group which consists of those atopic patients who have suffered from rhinitis and bronchial asthma since their earliest childhood, and (2) the smaller group comprising the nonatopic patients who remain symptom-free until relatively late in life, when nasal polyps and bronchial asthma develop without warning and progress rapidly.

Atopic and nonatopic patients who develop nasal polyps present, at first glance, a similar clinical picture and their complaints are almost identical. Yet, it is likely that they represent diseases of different causation. As a matter of fact, the differences which we have observed have outnumbered the similarities. A well controlled atopic patient will, as a rule, respond to a comprehensive antiallergic regimen with decided improvement, often with complete freedom from symptoms. The elderly patient who develops nasal polyps and bronchial asthma will never respond to control, rarely to treatment, and will be subject to asthmatic episodes of increasing severity. Acetylsalicylic acid relieves the atopic individual; yet, strikingly, it is likely to cause fatal attacks in the elderly patient with "intrinsic" respiratory disease.

For successful management of nasal polyps, one must realize that polyps may in some instances be limited to the nasal mucous membrane, but that more often than not they suggest similar changes in one or all of the neighboring nasal accessory sinuses. Rhinologists have often wondered why in some patients a simple removal of polyps by snare is followed by complete alleviation of symptoms and nonrecurrence of polyps, whereas in others, even repeated procedures and more extensive exenteration of the sinal mucosa produces debatable therapeutic results.

The group classification proposed by Samter offers a clue as to why some patients do respond to accepted surgical procedures and others do not. Rhinologists have wavered between so-called conservative and radical intranasal, and even external, sinus surgery. The enthusiasm for allergic management reflects, I believe, the awareness that failures from the more complete, or what Simonton calls more "comprehensive," forms of sinus surgery are not uncommon. Time does not permit a comparison between the effectiveness of adequate drainage and extensive surgery with the effectiveness of antiallergic management. I only wish to re-emphasize the fact that the nasal and sinal involvement represents the local manifestation of a constitutional disease.

What would I do then? In an atopic person who suffers from seasonal and perennial rhinitis associated with extensive nasal polyps, I would insist on rigid environmental control, recommend immunization to inhalants which cannot be avoided, perform a submucous resection of the nasal septum if the airways are significantly obstructed, or carry out additional operations on the nose and paranasal sinuses as dictated by clinical and roentgenographic evidence. The results of inadequate operation are as unsatisfactory as the results of inadequate antiallergic management.

In nonatopic persons, I would be inclined to be conservative and to postpone an operation as long as possible. It should be said, however, that the use of corticosteroids unfortunately does not represent the final therapeutic solution for the handling of nasal polyps. Many of you will certainly agree with me that symptomatic administration of hormones might restore nasal mucous membranes to seemingly normal appearance and function, but that upon withdrawal, nasal polyps inevitably recur.

KENNETH L. CRAFT, M.D., Indianapolis: To me, at least, the treatment of nasal polyposis, with its constant tendency toward recurrence, is one of the discouraging features of rhinologic practice. Most polyps, I believe, especially those of the multiple bilateral type, are either due to, or associated with, allergic disease of the nose and sinuses. Effective treatment of the allergic factor, in my own experience, at least, frequently has been successful in controlling the milder form of polyposis in which the polyps were relatively small and few in number. However, allergic management alone often fails to give the desired relief in the extremely severe and more extensive form of this disease. This type of case usually is due either to primary chronic infection alone or to secondary infection superimposed upon primary allergic disease, and

for lasting relief it often will require extensive radical surgery of the sinuses, as so well described in Dr. Simonton's fine discussion.

Dr. Simonton does not state what percentage of his cases was purely allergic, what percentage was purely infectious, nor how many cases were of the combined type. Perhaps this sort of classification might be of help in an appraisal of his over-all results. It might explain why such excellent results were obtained in 62 to 74 per cent of the cases which may have been infectious in their origin, and why recurrences developed in 26 to 38 per cent in which allergy may have been the cause.

Dr. Simonton does not mention the use of allergic treatment in any of his cases. Perhaps some of them would have responded to allergic treatment alone; I have seen this happen. Hitherto it has been taught that radical sinus surgery is contraindicated for the removal of allergic polyps, unless the case is complicated by chronic infection. In this mixed type of case the best results are obtained, I believe, by supplementing necessary surgical measures by adequate allergic treatment started before surgery is performed and continued postoperatively.

In general I feel that the type of treatment to be used in nasal polyposis depends largely upon the proper etiologic classification of the polyp, i.e., whether it is caused by allergy or by infection. I believe that the cause of a polyp can be established by biopsy. Dr. Simonton says (quoting from Taillens), "Tissue eosinophilia is not a constant finding and is of little clinical significance." I cannot subscribe wholeheartedly to this view. There is a marked difference between the allergic polyp and the infectious polyp. Differentiation between these two distinctive types can be made by biopsy. The infectious polyp will show a preponderance of neutrophils, but the allergic polyp is readily identified by the presence of edema, a preponderance of eosinophils, and hyalinization of the basement membrane. I feel that this differentiation must be made before the proper type of treatment can be determined, whether it be surgical, medical, or combined.

Any information which will shed more light upon the management of the troublesome problem of nasal polyposis should be very welcome to all of us. Dr. Simonton has added a distinct contribution to the subject and we are indebted to him for giving us the benefit of his work and experience in this field.

FREE SKIN GRAFTS AND PEDICLE FLAPS IN THE REPAIR OF NASAL DEFECTS

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THE purpose of this paper is to consider the handling of patients who have defects of the external nose requiring free skin grafts or pedicle flaps in their reconstruction.

Such defects result from a variety of causes. Although inflammatory diseases may produce this type of defect, the majority of them today are the result of accidental injury, acts of violence, or treatment for malignant tumors.

Many comprehensive articles on the subject by outstanding surgeons are available in the literature, and many creditable exhibits and demonstrations are seen from time to time. A brief review of the literature will be followed by reports of cases from the author's personal experience. One of the cases will be reported in some detail. According to Padgett,[8] a description was recorded in India centuries ago of the free transplantation of full-thickness skin from the gluteal region to the nose.

In the first third of the nineteenth century Bunger of Marbury successfully transplanted a free piece of whole skin from a woman's thigh to her nose. In the middle third of the century J. Mason Warren of Boston became known for his work in this field. In the last third of the century interest in free grafts became general as a result of the work of Reverdin, Ollier, Thiersch, Wolf, Krause, and others.

In 1929 Blair and Brown[2] described the use of their special suction box and knife blade for obtaining split-thickness skin grafts.

Between 1930 and 1937 Padgett,[8] with the help of Hood, was developing the dermatome, which more or less revolutionized the use of free skin grafts. More recently the electric dermatome has gained popularity with a number of surgeons.

According to New and Erich,[7] the earliest known descriptions of pedicle flaps were in the Egyptian papyri from 3000 to 2500 B.C. In 1000 B.C. the Hindu Susruta made a similar report.

In 1597 Tagliacozzi's book *De Cortutum Chirurgia* was published. In it he described the delayed arm flap for nasal reconstruction.[3,5]

In October 1794 *Gentlemen's Magazine*, an English lay journal, contained a detailed description of the ancient Indian operation for reconstruction of the nose with a pedicle flap from the forehead. The patient had been a bullock driver with the English army in 1792, and his nose and one of his hands had been cut off following his capture.

No further significant development seems to have taken place in this field until the twentieth century.

While long pedicle flaps tend to tube themselves, the first report to the medical profession describing this as a surgical technique seems to have been made by Filatow of Odessa in 1916.[1] However, Sir Howard Gillies of London was chiefly responsible for its widespread popularity which developed soon afterwards.

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The position of the nose has forever exposed it to accidental injury and acts of violence. The practice of mutilating the nose as a means of punishment as well as for ceremonial purposes has been carried out in many parts of the world for an extremely long time. According to Humfreville,[4] while the Apache Indians of the southwest United States were polygamous, they were very rigorous in regard to the fidelity of their wives. Any infraction of this code was punishable by shaving off the nose of the offending woman close to the face.

Nasal deformity has also resulted from a number of inflammatory diseases.

It appears that there has been a significant need for reconstructive surgery of the nose since long before recorded history, and one wonders how long these needs may have been met in some degree.

The choice of a graft with which to reconstruct any particular defect depends on many complex factors. Consequently, competent surgeons do not always agree except on general principles.

In the opinion of the author it is usually advisable to use a method that promises to result in the best appearing nose with a minimum of exposed scarring from the donor area. The use of unnecessary operative procedures is not wise. However, the advantage of having the best final result usually justifies the additional procedures when the method requires them.

A free skin graft can be used when there is no significant loss of lining of the nasal cavity.

A thick split skin graft is probably the best in most cases. Since the graft is relatively small, the chance of a take is good. There is no advantage and some disadvantage in using a very thin graft, and it is usually not necessary to use a full-thickness graft. However, occasionally when the defect is deep a full-thickness graft may be better, and if it is deep enough, a pedicle flap may be justified.

The graft may be taken from the postauricular region, upper arm or thigh. Interrupted silk sutures are left long and tied over fluffed gauze for firm even pressure for a period of eight to ten days. Some surgeons dress these wounds as early as the fifth day.

The selection of a flap is more complicated, since there is a much wider choice and the matter of lining has to be taken into consideration.

If the defect is small enough, the margin can often be turned in for lining. When the ala is involved, the graft may be turned upon itself for the lining if the defect is not too large. In larger defects the pedicle graft must be lined with a split-thickness free graft ten days or two weeks before it is transferred.

Flaps from the cheek leave some additional scarring and should be used only when this is acceptable. The same is true of forehead flaps, especially in bald men. Women may be able to dress the hair so that the scars are covered.

The sickle shaped flap described by New[6] is very useful in people with plenty of hair, for most of the flap is raised from back of the hair line and only the part that is actually used comes from the exposed forehead.

The delayed arm flap is not popular because of the poor color match and the uncomfortable position that must be maintained.

The color match is usually best with grafts from near by.

Whenever part of the blood supply to a skin flap is interrupted the remaining supply is stimulated to increase. This principle, known as delaying, was used by Tagliacozzi. It is useful when it is necessary to increase the nourishment passing through the pedicle to a relatively large flap. This is brought about by

incision and resuturing in the original location of parts of the flap. This is done in stages from one to three or more weeks apart.

The smaller pedicle flaps that have a rich blood supply, as in the supraorbital region, can often be transferred without delay unless a free graft is required for a lining. The larger flaps with the pedicle in the preauricular region, for instance, usually require delay.

When skin from an unexposed area, such as the clavicular region, is to be used, the flap is usually tubed when it is first elevated, a pedicle being left at each end. This reduces the exposed raw surface to a minimum. The length of the flap should not be more than three times its width so that the blood supply will be adequate throughout. Six to ten weeks later one end of the flap is cut across in two stages and attached high on the neck. This step is necessary so that the other end will reach the nose.

About two weeks later the donor end is cut half across. In another ten days or two weeks it is transferred to the region of the nose. If a lining is necessary, a free split-thickness graft can be applied when the donor end is first cut half across. At least three weeks is required for the blood supply through the attachment to become sufficient so that the tube can be excised in stages ten days or two weeks apart and discarded.

The following cases illustrate most of the above points.

CASE REPORTS

Case 1

This 49-year-old man had been treated intermittently for eight years with roentgen rays and radium. The original lesion had been a small pimple on his nose (fig. 1,A). On January 18, 1954, this entire area of actinodermatitis was excised. Frozen section proved the presence of basal cell epithelioma, but since the margin and depth appeared adequate microscopically, a free split-thickness graft from the upper arm was applied. Three years later there was no evidence of recurrence (fig. 1,B).

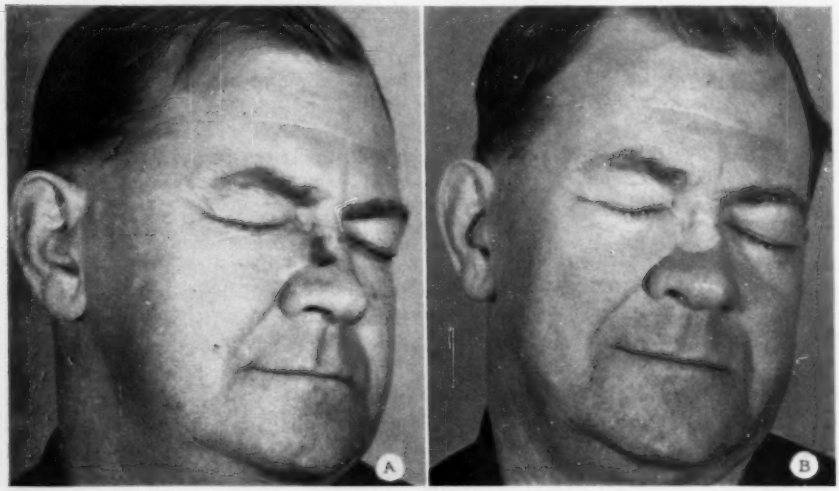

FIG. 1—Case 1. (A) Actinodermatitis with basal cell epithelioma. (B) Appearance three years later.

Case 2 [Slide]

This woman had had a persistent ulcerative lesion on the dorsum of the nose which was excised and covered by a simple rotation

flap from the nasolabial fold and dorsum of the nose after frozen sections revealed no evidence of carcinoma.

Case 3 [Slide]

This man was referred for plastic repair after having had irradiation and electrocoagulation for carcinoma of the nose. The sequestrum of bone was removed and the defect covered with a pedicle flap from the forehead. This defect could have been covered with a free graft but there would have been a resulting depression. A midline forehead flap could have been used here. Small forehead defects can be closed without a graft.

Case 4. [Slide]

Defect resulting from removal of basal cell carcinoma involving skin of the nose, nasal septum and nasal cartilages. Ten months later it was covered with a lined sickle-shaped pedicle flap from the forehead and scalp. There has been no recurrence in nine years.[9]

Case 5

This man was in a fight and was getting the better of it until the loser bit part of his nose off (fig. 2). Because of the likelihood of keloid formation it was thought unwise to repair the defect with tissue from an exposed area. Consequently, a flap was tubed in the

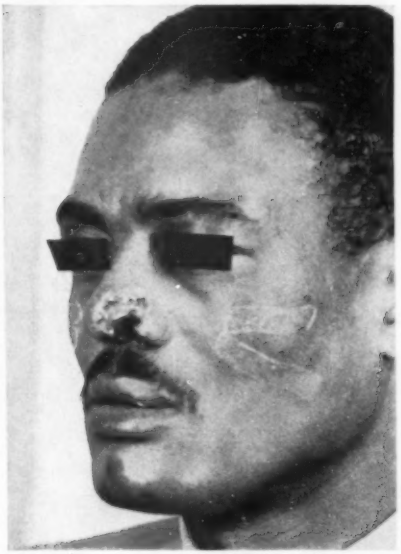

FIG. 2—Case 5. Nasal defect due to human bite.

FIG. 4—Case 5. Final result of grafting procedure.

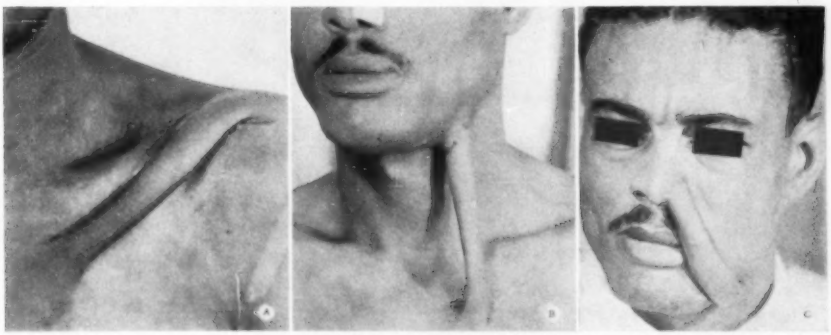

FIG. 3—Case 5. (A) Tubed clavicular flap. (B) Upper end of flap attached high on neck. (C) Donor end of flap attached to the nose at site of defect.

left clavicular region (fig. 3,A). It was brought up in stages (fig. 3, B and C). The dark appearance of the graft is due to increase of pigment (fig. 4). This is a common occurrence when pedicle grafts are applied to the noses of colored people. The increase in blood supply is no doubt a factor.

Case 6 [Slide]

This man had had irradiation of the left nasal alar region for squamous cell carcinoma, grade 2. Extensive electrocoagulation was necessary to treat a recurrence. Several precancerous lesions and one other squamous cell carcinoma were removed from the face. This eliminated the cheeks as donor areas, and since the patient was bald, it was decided to use a clavicular tube flap. Difficulty with the flap necessitated an intermediate stage during which it was attached to the cheek, but the reconstruction was completed.

FIG. 5—Case 7. Basal cell carcinoma with perforation into nasal cavity.

Case 7

In the summer of 1943, while teaching swimming, this woman developed a small blister on the dorsum of her nose from sunburn. The lesion remained, and in 1945 her doctor made a diagnosis of discoid lupus erythematosus. Bismuth therapy was begun. She was under treatment and regular observation for several years.

In 1948, following an automobile accident, she developed a subdural hematoma. Several trephine openings were made in the skull in the course of treatment which followed. Later in 1948 she was put on cortisone therapy (4 tablets a day), and this was continued until 1951, at which time Atabrine was prescribed.

In 1954 the patient's dentist questioned the original diagnosis and urged consultation. A biopsy by Dr. C. E. Reyner revealed mixed basal and squamous cell carcinoma.

The patient was referred to me, and I found that she already had a perforation through the dorsum of the nose into the nasal cavity (fig. 5).

FIG. 6—Case 7. (A) Defect following electrocoagulation of tumor of nose, tubed clavicular flap. (B) Upper end attached high on neck and donor end lined with free skin graft. (C) Lined donor end attached at site of defect.

In January 1957 the tumor was removed with the diathermy knife and the defect electrocoagulated. At the same time a tumor was removed from the right forearm. This also proved to be mixed basal and squamous cell carcinoma. It was thought that this tumor probably resulted from contact of the arm and nose during sleep.

It seemed undesirable to scar the cheeks or forehead in making the repair, and scarring from the trephines ruled out a sickle-shaped flap. Consequently, in November 1955, ten months after destruction of the tumor, repair of the defect was started by use of a tubed pedicle flap from the right clavicular region (fig. 6,A).

FIG. 7—Case 7. Final result of grafting procedure.

Ten weeks later, the upper end of the tube was cut half across and resutured. In another two weeks it was cut completely across and attached to the upper neck. About two weeks later the lower end of the flap was lined with a split skin graft from the abdomen (fig. 6,B).

After two partial excisions with an interval of two weeks between them, the nasal defect was freshened and the lined graft attached to it (fig. 6,C).

On April 17, twenty-eight days later, the tube was partially excised close to the defect. On April 26, nine days later, it was completely excised and discarded. The skin of the nose was sutured to the free skin edge of the flap. No further shaping up has been necessary.

The photograph shows the appearance of the graft in August 1956, four months later (fig. 7).

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DISCUSSION

JOHN B. ERICH, M.D., Rochester, Minnesota: Dr. Weaver has given us a well-organized outline of skin grafts needed for the repair of various defects of the nose. I wish to emphasize the fact that free skin grafts, that is, shave (Thiersch, split-thickness) and full-thickness (Wolfe, dissected) grafts have a limited degree of usefulness in nasal surgical repair because they can be employed only on superficial surface defects. Such free skin transplants cannot be expected to heal properly in tissues in which the blood supply is inadequate because of previous irradiation or excessive scarring, and cannot be employed over a hole or perforation which has no blood supply at all.

If a superficial loss of skin on the nose is not too large, a full-thickness skin graft dissected from the posterior auricular region is

highly desirable because of its color, texture and thinness. However, when the surface defect is large or involves the whole nose, sufficient skin cannot be obtained from behind the ear. Under these circumstances, one is forced to use a shaved skin graft or a full-thickness graft from the neck, trunk, or limbs. The only full-thickness graft obtained from these regions which has a satisfactory color is one taken from the supraclavicular region. However, any full-thickness graft obtained from the neck, trunk or limbs is likely to be too thick and is inclined to slough when placed over the nose. Notwithstanding the fact that shaved or split-thickness skin grafts often are too white or may become pigmented, I prefer them to full-thickness grafts from the neck, trunk or limbs because the former are thin and usually heal very satisfactorily.

The majority of nasal defects require a pedicle flap of skin for repair, the flap having its own blood supply through the pedicle. In the repair of any defect on the nose, one always should consider using one of three types of pedicle flaps: (1) contiguous flaps, which are elevated immediately adjacent to the nasal defect; (2) neighboring flaps, which for nasal surgery are elevated on the forehead or along the nasolabial fold; and (3) distant flaps, which when used for nasal repair are tubed pedicle grafts elevated over the clavicle or on the anterior chest wall.

In area and outline there are no standards for contiguous flaps; they vary in accord with the shapes and locations of the nasal defects. For a small loss of tissue on the nose, contiguous flaps offer the quickest method of repair. Moreover, their color and texture are the same as those of the rest of the nose, since they are derived from the tissues adjacent to the defect. However, contiguous flaps have a limited degree of usefulness, since they can be employed only for small perforations or losses of skin and can be elevated only in tissues which are not changed by irradiation and which are not excessively scarred.

Unless the skin over the frontal region is scarred, the use of a neighboring flap on the forehead is always to be considered for repair of defects too large to be corrected by contiguous flaps. Forehead flaps require less time in preparation, are less difficult to prepare and are less likely to slough than any of the distant tubed flaps on the chest. Moreover, forehead flaps give excellent cosmetic results in that the color and texture of the skin are similar to the dermal covering of the nose. They do have one distinct disadvantage: they leave conspicuous scarring at the donor site on the forehead—a fault which has brought me to the point of almost discontinuing their use.

The neighboring flaps on the forehead which I use in repairing the nose are of three types: a sickle-shaped temporal flap with a pedicle in the preauricular region, a vertical forehead flap which can be elevated from along the midline or over one brow, and a loop-shaped supraorbital flap with a pedicle over one brow.

A sickle-shaped temporal flap may be used effectively in reconstructing partial defects of the nose and leaves less residual scarring than any of the other forehead flaps. However, a sickle flap never provides enough tissue for total nasal repair or for reconstruction of the lower half of the nose.

A vertical flap on the forehead, whether elevated from the center of the forehead or from over one brow, offers the most rapid means of correcting certain types of nasal defects. But unless the patient is bald, such a flap is of limited length and consequently is usable only for defects of the upper half of the nose. Furthermore, it frequently leaves conspicuous scars on the forehead, and I do not recommend it except for individuals who want their nasal defect repaired as quickly as possible and are not concerned with such scars.

For total nasal reconstruction, a loop-shaped forehead flap is excellent because the color, texture and thickness of the skin over the forehead are perfectly adapted for building an entire nose. However, such a flap leaves a great deal of conspicuous scarring at the donor site on the forehead, and I have been inclined in recent years to use a distant flap elevated and tubed over the clavicular region or on the anterior chest wall.

I have found that an excellent nasal reconstruction can be achieved with a clavicular tube flap or the upper end of a chest tube flap which has good color and texture. The great advantage of either a clavicular or a chest tube flap lies in the fact that the scarring at the donor site is not visible when the patient is clothed. The only real disadvantage of a tube flap is that a longer period is required to complete the nasal reconstruction than is necessary with a forehead flap. Consequently, only for patients who are not concerned with a scarred forehead and who want the reconstruction done as quickly as possible do I use a forehead flap. Otherwise, at present I prefer a clavicular or chest tube flap.

AN INVESTIGATION OF THE LONG-TERM EFFECTS OF FENESTRATION SURGERY ON AUDITORY NERVE DEGENERATION

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BY INVITATION

THE following presentation is a portion of a broader investigation of otosclerosis and some auditory effects of fenestration surgery.* The subject to be discussed below comes from that portion of the total investigation which was designed to answer the question: What is the effect of fenestration surgery upon progressive nerve degeneration?

Woods[10] and Juers[3] observed improvement in the bone conduction thresholds of the ear on which the operation was done. This observation was repeated in studies by McConnell[6] and Henner,[2] who suggested improvement at least at 1,000 to 4,000 cycles and up to three months postoperatively. At the same time, statements in the literature implied that fenestration surgery had an effect upon cochlear functioning by means of a retardation of the progression of secondary nerve degeneration,[1,4,5,8] and as recently as 1955, Shambaugh[9] stated that "this unexpected (and still questionable) benefit of the operation needs to be confirmed or disproved by future long-term studies." The present investigation was designed to evaluate these two problems statistically over a longer period of time than had previously been reported.

*Feldman, A. S.: An Investigation of Several Auditory Effects of the Fenestration Operation for Otosclerosis. Unpublished doctoral dissertation, Syracuse University, 1956.

Presented at the *Special Program* of the Otosclerosis Study Group and the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology, Oct. 13, 1957, Chicago.

SUBJECTS AND PROCEDURES

The experimental group of subjects was composed of 99 patients who had undergone a unilateral fenestration operation at least five years prior to the current investigation. The mean duration of time lapse between the operation and test was 7.44 years and ranged from five to twelve years. There were 28 males and 71 females, and the over-all mean age was 41.15 years. The control for each subject was the contralateral, nonfenestrated ear. Subjects were serially selected as they returned to the Winthrop Foundation for their postoperative visits.

For each subject, threshold measures of pure tone air conduction, bone conduction, and speech reception were obtained, as were discrimination scores. The records of all subjects contained similar preoperative measures and, with the exception of the speech tests, which were not comparable, these measures were used as a basis of comparison of fenestrated and nonfenestrated ears preoperatively to postoperatively. Testing routine was rigorously adhered to in terms of order of tests and masking.

DISCUSSION OF RESULTS

The subjects were classified according to the results of surgical operation, and all analysis was based upon intergroup differences as well as differences between the ears that had been operated upon and those which had not. Classification of the subjects was in terms of the tradi-

TABLE 1

CLASSIFICATION OF SUBJECTS ON THE BASIS OF THEIR POSTOPERATIVE HEARING STATUS: SHOWING NUMBER (N), PERCENTAGE, MEAN AGE, AND AGE RANGE FOR EACH GROUP

CLASSIFICATION	N	PERCENTAGE	MEAN AGE	AGE RANGE
Successful	52	52.5	41.00	24-65
Improved	21	21.2	43.33	21-63
Failure	26	26.3	39.69	21-65
Total	99	100.0	41.15	21-65

tional successful, improved, and failure categories used in the literature.[7] Table I is a summary of the postoperative groupings. The successful group constituted 52.5 per cent of the total, while the improved group comprised 21.2 per cent and 26.3 per cent were classed as failures. Ages were fairly constant for each group.

The changes in air conduction for each group are depicted in figure 1. As might be anticipated, the successful group gained 23.79 decibels, while the failure group continued to add to its preoperative loss, dropping 3.00 decibels from its preoperative level. The improved group had a gain of 17.14 decibels, a surgical success but insufficient for practical hearing. Thus, the ear for which the operation is considered a fail-

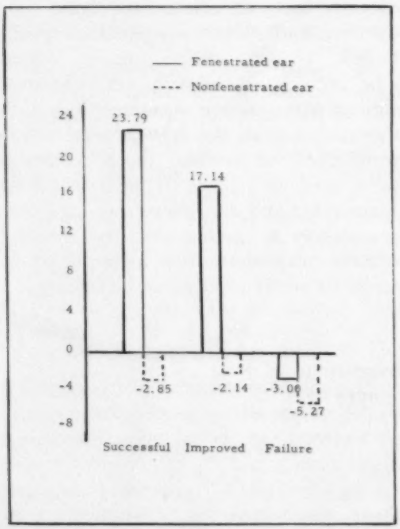

FIG. 1—The relative preoperative decibel change minus the postoperative decibel change for each category for air conduction.

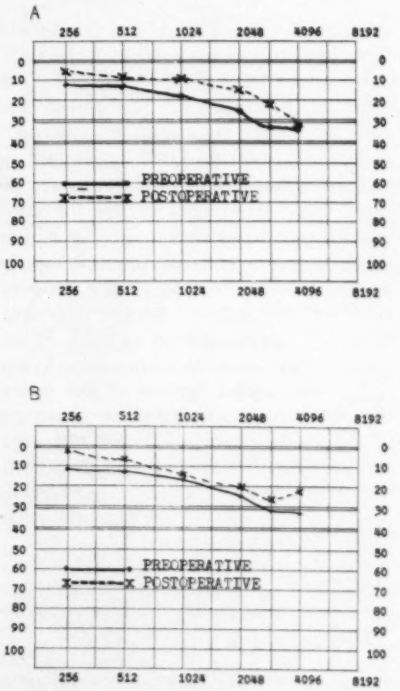

FIG. 2—Mean bone conduction thresholds, preoperatively and postoperatively for (A) fenestrated ear and (B) nonfenestrated ear.

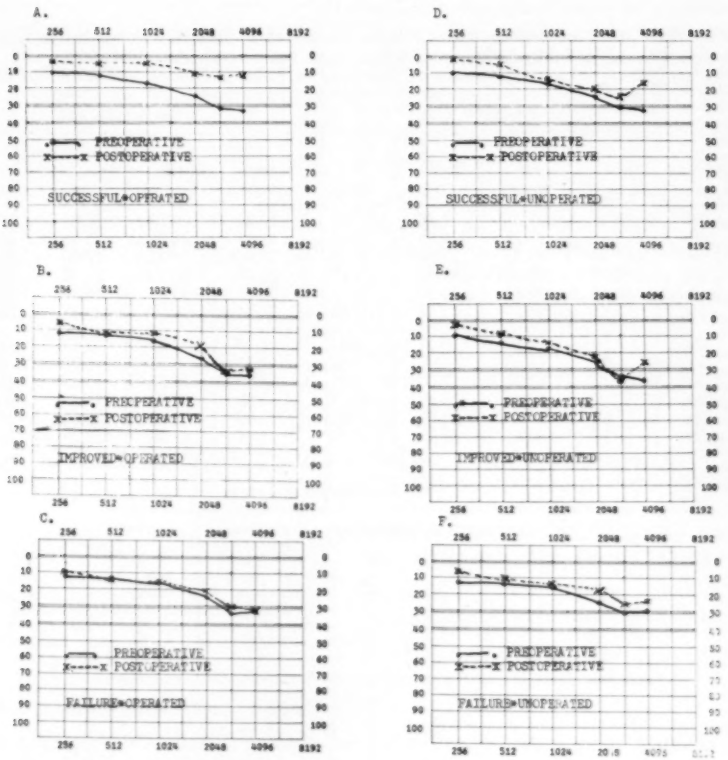

FIG. 3—Mean bone conduction thresholds, preoperatively and postoperatively for (A) successful category fenestrated ear, (B) improved category fenestrated ear, (C) failure category fenestrated ear, (D) successful category nonfenestrated ear, (E) improved category nonfenestrated ear and (F) failure category nonfenestrated ear.

ure resembles the unoperated ears of all groups in its progression. There is no statistical evidence of improvement in the air conduction of the unfenestrated ear; it continues to drop postoperatively.

The bone conduction findings were statistically analyzed from two departures. The first was a direct comparison of the mean bone conduction thresholds for each ear preoperatively to postoperatively (fig. 2). In each instance the bone conduction postoperatively shows mean values that are better than the preoperative thresholds, though thresholds for the fenestrated ears are better by a larger amount. The data could scarcely be interpreted as indicative of any progression of hearing loss in the ear not surgically treated. Statistical analysis, as well as visual inspection, confirms this observation. The major source of changes in threshold may be observed by a breakdown of the data into thresholds according to the effectiveness of surgical procedures (fig. 3). A comparison is made between the preoperative and postoperative states of each ear. The major difference is clearly noted in the fenestrated ear in successful

TABLE II

PREOPERATIVE AND POSTOPERATIVE MEAN BONE CONDUCTION THRESHOLDS FOR EACH EAR AT 250, 500, 1,000, 2,000, 3,000, AND 4,000 CYCLES FOR SUCCESSFUL, IMPROVED, AND FAILURE GROUPINGS WITH THE NUMBER OF SUBJECTS IN EACH CATEGORY FOR EACH FREQUENCY

		OPERATED EAR				UNOPERATED EAR			
	FREQUENCY (CYCLES)	SUCCESSFUL	IMPROVED	FAILURE	TOTAL	SUCCESSFUL	IMPROVED	FAILURE	TOTAL
Preoperative	250	10.68	11.38	11.73	11.11	10.34	9.72	12.82	10.88
	500	12.35	13.25	12.88	12.68	12.84	13.75	13.46	13.09
	1,000	18.26	18.33	17.69	18.13	18.46	18.33	17.50	18.18
	2,000	25.78	28.09	25.38	26.17	25.09	26.19	25.38	25.40
	3,000	31.73	35.83	33.50	33.22	30.43	33.33	30.50	31.22
	4,000	33.33	36.31	31.52	33.50	32.44	36.57	29.38	32.64
Postoperative	250	3.18	7.50	10.21	6.00	1.13	2.50	6.52	2.88
	500	4.60	12.50	14.42	8.86	4.21	9.50	11.92	7.37
	1,000	4.23	12.61	17.30	9.44	13.65	15.71	15.00	14.44
	2,000	11.37	19.04	20.19	15.35	19.80	23.57	18.27	20.20
	3,000	13.91	34.58	29.50	22.88	23.69	36.66	26.50	27.77
	4,000	12.55	34.47	31.30	32.29	17.44	27.36	23.26	21.14

FREQUENCY (CYCLES)	NUMBER OF SUBJECTS			
	SUCCESSFUL	IMPROVED	FAILURE	TOTAL
250	44	16	23	85
500	51	20	26	97
1,000	52	21	26	99
2,000	51	21	26	98
3,000	23	12	10	45
4,000	45	19	23	87

cases, although some improvement is to be observed in all instances at 250 cycles, and frequently at 500 cycles.

Statistical analysis of the changes in mean decibel differences reveals significant F scores at 250 ($F=7.04^{**}$), 500 ($F=3.88^{*}$), 1,000 ($F=22.94^{***}$), 2,000 ($F=17.00^{***}$), and 3,000 cycles ($F=7.14^{**}$). Thus, at none of these frequencies would the changes be considered due to chance, according to rigorous levels of statistical probability. Furthermore, the group differences which imply that the major differences in threshold are due to improvement in the successful category (fig. 3) were also statistically confirmed. Thus, rather than statistically significant progression of hearing loss in nonfenestrated ears, what we observe is statistically significant improvement in bone conduction for successfully fenestrated ears (table II).

In no instance do postoperative thresholds by bone conduction exceed the values of the preoperative thresholds by more than 3 decibels. These data would fail to support the contention that even in nonfenestrated ears there is a progressive degeneration of the nerve which may be observed after a mean duration of 7.44 years, the mean duration of time between measurements in this study. The distinct difference between preoperative bone conduction thresholds in successful cases and subsequent postoperative thresholds as compared to minimal difference observed in all other categories strongly reinforces the findings of other workers[2,6] that there is a bone conduc-

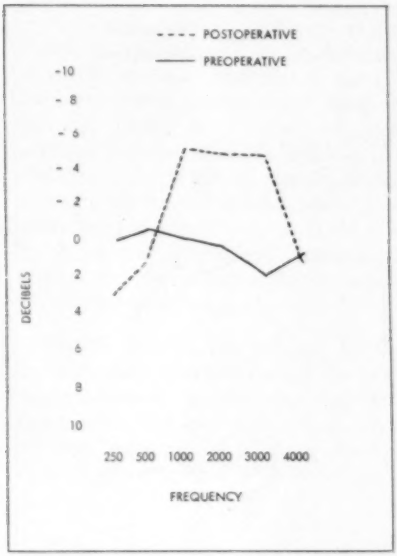

FIG. 4—All categories: the differences between fenestrated and nonfenestrated ears preoperatively and the differences between fenestrated and nonfenestrated ears postoperatively at 250, 500, 1,000, 2,000, 3,000, and 4,000 cycles, bone conduction.

tion threshold improvement following fenestration. One might speculate that differences which have previously been observed in bone conduction measurements between surgically treated and nonsurgically treated ears and which have been interpreted as an indication of progression in the ear not surgically treated might instead have been an indication of the improvement in the surgically treated ear. The lack of a poorer postoperative threshold in nonfenestrated ears for the sample studied would lend support to the latter contention.

Analysis of the data by means of comparing the difference between the fenestrated and the nonfenestrated ears postoperatively reinforces this position (fig. 4). A difference in the negative direction would imply a greater loss in the ear not surgically treated whereas a positive value would imply a greater loss in the ear which had been operated upon. Figures 5, 6, and 7 present the successful, improved and failure categories respectively. The marked differences which are implied by the examination of these figures are verified by statistical analysis of the data.

At 250 cycles the F value of 7.04 for preoperative mean differences and postoperative mean differences is significant at the .01 level of confidence. The values for the preoperative differences of 0.34 decibels, 1.67 decibels, and –1.09 decibels, and an over-all mean difference preoperatively of 0.24 decibels are compared with a postoperative difference of 2.05, 5.00, and 3.70 decibels in the successful, improved, and failure categories respectively, and an over-all decibel difference postoperatively of 3.12. The major source of this difference lies in the improved and failure categories,

FIG. 5—Successful category: the differences between fenestrated and nonfenestrated ears preoperatively and the differences between fenestrated and nonfenestrated ears postoperatively at 250, 500, 1,000, 2,000, 3,000, and 4,000 cycles, bone conduction.

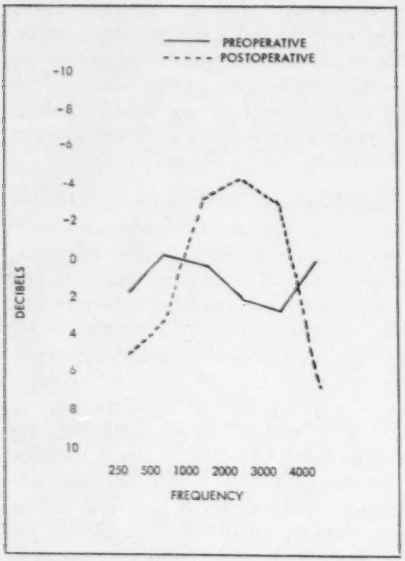

FIG. 6—Improved category: the differences between fenestrated and nonfenestrated ears preoperatively and the differences between fenestrated and nonfenestrated ears postoperatively at 250, 500, 1,000, 2,000, 3,000 and 4,000 cycles, bone conduction.

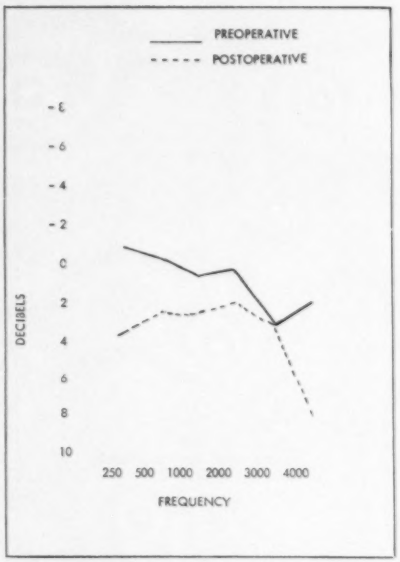

FIG. 7—Failure category: the differences between fenestrated and nonfenestrated ears preoperatively and the differences between fenestrated and nonfenestrated ears postoperatively at 250, 500, 1,000, 2,000, 3,000, and 4,000 cycles, bone conduction.

whereas the difference for a successful category is only 1.71 decibels. Despite this, the analysis of variance between groups reveals an F of 1.52, which is not significant. Table III is a summary of the mean differences preoperatively and the mean differences postoperatively at each frequency for all groups, and the analysis of variance. Very similar results were obtained at 500 cycles, where the preoperative mean differences were –0.49, –0.50, and –0.58 in successful, improved, and failure categories respectively, with an over-all mean of 1.49 decibels. The difference is smaller than it was at 250 cycles, and analysis of variance between preoperative and postoperative data yields an F of 3.88, which only approaches the 0.05 level of significance. Again the F's for group and interaction are not significant.

These significant and near significant variations at 250 and 500 cycles are difficult to account for. At 250 cycles, the data suggest that for successfully fenestrated ears there is some improvement, although there is also some indication that the differences are due to poorer hearing in failure cases. It has been suggested that these observed differences are due to some inherent difficulties in masking, while for the failure categories it might be related to postsurgical labyrinthitis.

At 1,000 cycles the marked change in the picture becomes evident. The obtained values for the preoperative mean differences in the successful, improved, and failure categories are –0.19, 0.00, and 0.19 decibels respectively, with an over-all mean difference of –0.05 decibels. This is opposed to the distinct differences postoperatively of –9.42, –3.10, and 2.31 decibels in the successful, im-

proved, and failure categories respectively, with an over-all mean difference of –5.00 decibels. Analysis of the preoperative versus postoperative mean differences yields an F score of 22.94, which is significant at the 0.001 level of confidence. In addition, the F of 8.45 between the groups is significant at the 0.001 level of confidence, as is the F of 10.98 of the interaction between the groups, and preoperative and postoperative differences.

For the data at 1,000 cycles there is a significantly greater hearing loss in the nonfenestrated ear for the successful cases, with the improved group about midway between the former and the failure group. This difference, which changes from group to group, is consistent with the previous findings of the mean threshold values preoperatively and postoperatively, where major differences were observed in the postoperative thresholds of successful cases.

Similar results were obtained for the 2,000 cycles data. In the successful, improved, and failure categories, the mean differences of 0.69, 1.90, and 0.00 decibels, with an over-all mean difference of 0.77 decibels, were obtained preoperatively. The respective values for the postoperative differences are –8.43, –4.52, 1.92, and –4.85 decibels respectively. These were found to be significant at the 0.001 level of confidence, with an F of 17.00. In addition, the difference be-

TABLE III

MEAN PREOPERATIVE, POSTOPERATIVE AND COMBINED DIFFERENCES FOR ALL CATEGORIES AT 250, 500, 1,000, 2,000, 3,000, AND 4,000 CYCLES AND RESULTS OF ANALYSIS OF VARIANCE

FREQUENCY	CATEGORY	N	MEANS			ANALYSIS OF VARIANCE		
			PREOPERATIVE	POSTOPERATIVE	COMBINED	$F_{PRE-POST}$	F_{GROUPS}	$F_{P \times G}$
250	Successful	44	0.34	2.05	1.19	7.04**	1.52	<1.00
	Improved	18	1.67	5.00	3.33			
	Failure	23	—1.09	3.70	1.30			
	Total	85	0.24	3.12	1.68			
500	Successful	51	—0.49	0.39	—0.05	3.88 (F.05=3.94)	<1.00	<1.00
	Improved	20	—0.50	3.00	1.25			
	Failure	26	—0.58	2.50	0.96			
	Total	97	—0.52	1.49	0.49			
1,000	Successful	52	—0.19	—9.42	—4.81	22.94***	8.45***	10.98***
	Improved	21	0.00	—3.10	—1.55			
	Failure	26	0.19	2.31	1.25			
	Total	99	—0.05	—5.00	—2.53			
2,000	Successful	51	0.69	—8.43	—3.87	17.00***	5.98**	5.83**
	Improved	21	1.90	—4.52	—1.31			
	Failure	26	0.00	1.92	0.96			
	Total	98	0.77	—4.85	—2.04			
3,000	Successful	23	1.30	—9.78	—4.24	7.14* (F.01=7.27)	2.37	1.58
	Improved	12	2.50	—2.08	0.42			
	Failure	10	3.00	3.00	3.00			
	Total	45	2.00	—4.89	—1.44			
4,000	Successful	45	0.89	—4.89	—2.00	<1.00	3.59*	4.82* (F.01=4.92)
	Improved	19	—0.26	7.11	3.42			
	Failure	23	1.74	8.04	4.89			
	Total	87	0.86	1.15	1.01			

F0.05=*; F0.01=**; F0.001=***.

TABLE IV

MEAN DIFFERENCES ($\bar{D}$), NUMBER (N), STANDARD ERROR OF THE DIFFERENCES (σ), DEGREES OF FREEDOM (df), AND t VALUES FOR THE SUCCESSFUL, IMPROVED, AND FAILURE CATEGORIES AT 500, 1,000, 2,000, AND 4,000 CYCLES

FREQUENCY	CATEGORY	N	$\bar{D}$	σ	df	t
500	Successful	51	0.88	1.24	50	<1.00
	Improved	20	3.50	2.54	19	1.38
	Failure	26	3.08	2.19	25	1.40
1,000	Successful	52	—9.23	1.48	51	6.23***
	Improved	21	—3.10	2.17	20	1.43
	Failure	26	2.12	1.91	25	1.11
2,000	Successful	51	—9.12	2.08	50	4.38***
	Improved	21	—6.43	2.89	20	2.22*
	Failure	26	—1.92	2.04	25	<1.00
4,000	Successful	45	—5.78	2.44	44	2.37*
	Improved	19	7.37	4.96	18	1.49
	Failure	23	6.30	4.40	23	1.43

***=t.001
*=t.05

tween groups is significant at the 0.01 level of confidence with an F of 5.98, as is the interaction F of 5.83.

The same tendency is observed at 3,000 cycles, where the F of 7.14 between differences is significant at the 0.05 level of confidence and approaches the 0.01 level of 7.27. For 3,000 cycles the preoperative mean differences are 1.30, 2.50, and 3.00 decibels in the successful, improved, and failure groups, with an over-all preoperative mean difference of 2.00 decibels. The postoperative means for the same categories are –9.78, –2.08, 3.00 and –4.89 decibels. Analysis of variance between groups and interaction is not significant. This lack of significance may be due to the considerably fewer subjects for whom the data were available at 3,000 cycles.

The mean differences were not as large at 4,000 cycles as for the lower frequencies, the means preoperatively being 0.89, –0.26, 1.74, and 0.86 in the successful, improved, failure, and over-all categories, and –4.89, 7.11, 8.04, and 1.15 in the same categories postoperatively. There is some implication in the data of greater losses in the fenestrated ears of both improved and failure groups postoperatively. This is the manifestation of indications of the air conduction data in another aspect of the study, which suggested possible surgical damage at 4,000 and 8,000 cycles in these groups. The analysis of variance between preoperative differences and postoperative differences results in an F of less than 1. The F of 3.59 between groups is significant at the 0.05 level of confidence, as was the interaction F of 4.82, again implying that preoperative differences to postoperative differences change significantly from group to group.

In addition to the analysis of variance, it was felt that it would be possible to investigate the differences preoperatively and postoperatively by investigating the null hypothesis that the mean difference equals zero. This analysis was carried out for the frequencies 500, 1,000, 2,000, and 4,000 cycles. Table IV summarizes the data in reference to this question and shows the mean differences, standard error of the differences, and the t scores.

In the successful group at 500 cycles the mean difference of 0.88 decibels is not significant. At 1,000 cycles the mean

difference rises sharply to –9.23 decibels and the resultant *t* of 6.23 is significant at the 0.001 level of confidence. Similarly, at 2,000 cycles, the *t* value of 4.38 for the mean difference of –9.12 is significant at the 0.001 level of confidence, while at 4,000 cycles the mean difference of –5.78 results in a *t* of 2.37, which is significant at the 0.05 level of confidence.

For the improved group the *t* is not significant for a mean difference of 3.50 at 500 cycles and –3.10 at 1,000 cycles, but at 2,000 cycles the mean difference of –6.43 results in a *t* of 2.22, which is significant at the 0.05 level of confidence. The mean difference of 7.37 at 4,000 cycles does not prove to be significant. The mean differences of 3.08, 2.12, and –1.92, and 6.30 decibels at 500 through 4,000 cycles are not significant for the failure group.

These data reinforce the impression that the differences observed in the successful group are highly significant and are the main contributors to the significant variation. The indication from the values obtained is either (1) that the thresholds of the ear not surgically treated are considerably poorer postoperatively and that subtracting this threshold from the theoretically constant threshold of the fenestrated ear gives the reason for the negative values, or (2) that the threshold of the nonfenestrated ear remains relatively constant and the negative values arise as a result of improvement in thresholds in the surgically treated ear.

The preoperative versus postoperative analysis would strengthen the latter position wherein it was observed that postoperative thresholds in successful cases are significantly better than preoperative thresholds in the ear to be fenestrated (fig. 3). This improvement may be compared to values obtained in separate studies by Henner[2] and McConnell,[6] who observed improvement in the bone conduction thresholds in fenestrated ears approximately three months after surgical operation. At 500, 1,000, 2,000, and 4,000 cycles, Henner found a mean improvement of 2.5, 8.7, 8.2, and 7.5 decibels respectively. For the same frequencies, McConnell observed improvement in the order of 2.5, 5.0, 8.0, and 5.0 decibels. The successful category in this study had a mean improvement, as implied by preoperative differences minus postoperative differences of –0.88, 9.23, 9.12, and 5.78 decibels for 500, 1,000, 2,000, and 4,000 cycles respectively. The mean differences for the entire experimental group were –2.01, 4.95, 5.62, and –0.29 decibels, in the same order. The resemblance is quite high for the middle two frequencies.

In the successful cases for the frequencies 1,000 through 4,000 cycles, there is clearly a much greater difference between ears, and this difference appears to be the result of improved thresholds for bone conduction. The subjects classified as improved demonstrated a similar improvement, but not to the degree experienced by the subjects in the category "successful." An effect upon the failure group becomes evident at 4,000 cycles, but this effect is in the direction of greater impairment of threshold.

SUMMARY

Ninety-nine subjects who had undergone a unilateral fenestration operation at least five years prior to their inclusion in this study were evaluated for changes in bone conduction. The subjects were considered as a group and were also categorized according to the effectiveness of the surgical operation. Differences between ears were observed to be on the basis of improved bone conduction postoperatively in the ears in which fenestration had been successful or in which hearing had been improved. There was no indication that there was a progres-

sive degeneration of the nerve either in ears not surgically treated or in ears in which the operation had failed, within the acknowledged limits of measurements of cochlear reserve by present bone conduction testing methods. The specific findings may be enumerated as follows:

Air Conduction Findings

1. There was no significant improvement in the air conduction thresholds of the ears not surgically treated; in fact, mean values were indicative of slightly increased hearing loss regardless of the effectiveness of surgical operation.

2. The fenestrated ear, when the operation failed, resembled the unoperated ear in all cases.

Bone Conduction Findings

1. There was a significant improvement in bone conduction thresholds above 500 cycles in a successfully fenestrated ear for as long as five to ten years following surgical operation. The mean improvement for successful cases was 9.23 decibels at 1,000 cycles, 9.12 decibels at 2,000 cycles, and 5.78 decibels at 4,000 cycles.

2. The improved category showed a similar but not as marked improvement in bone conduction thresholds. The mean change was an improvement of 3.10 decibels at 1,000 cycles, 6.42 decibels at 2,000 cycles, and greater impairment in the order of 7.37 decibels at 4,000 cycles.

3. Failures demonstrated no significant changes above 500 cycles.

4. Bone conduction thresholds above 500 cycles in the ear not surgically treated did not differ significantly preoperatively to postoperatively.

5. The mean differences preoperatively, when compared with the mean differences postoperatively, implied a greater impairment in the improved and failure categories at 250, 500, and 4,000 cycles than did the successful categories. This impairment could possibly be due to (a) techniques of masking for bone conduction audiometry, or (b) a physiological reaction secondary to labyrinthitis in the fenestrated ear of these subjects.

6. In general, there is no significant deterioration of bone conduction observed in this sample in the ear not surgically treated, when preoperative and postoperative thresholds are compared.

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DISCUSSION

GEORGE E. SHAMBAUGH, JR., M.D., Chicago: Dr. Feldman has attacked a very interesting and very important aspect of otosclerosis, namely, the nerve degeneration that so often complicates the stapes ankylosis.

We have no problem in accounting for the conductive loss of otosclerosis on a mechanical basis, and by means of stapes mobilization, supplemented when necessary by fenestration, we can expect to restore permanently the major part of the conductive loss in at least 90 per cent of cases. On the contrary, for the perceptive loss of otosclerosis not only can we do nothing but we do not understand exactly how it comes about. Nager and Fraser (J. Laryng. & Otol., 53:173-180, 1938) described an actual invasion of the cochlear perilymph space by otosclerotic bone, and this may account for a small percentage of the localized nerve losses seen in otosclerosis. However, in most of the ears with otosclerosis studied histologically, the cochlea is not invaded. In 1911 Siebermann observed a serous exudate in the perilymphatic space of the cochlea in several cases of extensive otosclerosis in which the focus had reached the endosteum of the cochlea. He suggested that the sensory nerve endings might be damaged by toxic substances liberated by the pathologic bone into the cochlear fluid. (Verhandl. der deutsch. otol. Gesellsch., 20:267, 1911)

The correctness of Siebermann's explanation for the usual nerve deterioration of otosclerosis is difficult to prove, although it seems to be the best that we have. Several clinical observations lend support to it. One is that nerve deterioration is usually greater in those patients with a strongly positive Schwartze's sign indicating a large and active otosclerotic focus. Another is that patients with advanced cochlear nerve degeneration sometimes develop additional symptoms of serous labyrinthitis with vertigo and diplacusis. Third, the perceptive loss of otosclerosis does not always continue to progress steadily but may stabilize after a period of progression, suggesting that the otosclerotic focus has become inactive with a cessation of toxic products liberated into the cochlea.

Another interesting observation is that fenestration may reduce or relieve tinnitus even when it does not change the hearing. This could be explained by an increased resorption of the toxic products from the perilymph afforded by the vascular skin flap over the fenestra. It could also explain the apparent effect of fenestration in retarding the nerve deterioration in some cases of otosclerosis. I say apparent effect, for the evidence so far is contradictory.

With some of Dr. Feldman's conclusions I agree completely. He has confirmed the fact first pointed out by Juers and later elaborated by Carhart that successful fenestration significantly improves the hearing by bone in the fenestrated ear, especially for the 1,024 and 2,048 frequencies. In 1950 McConnell made extremely carefully controlled measurements by air and bone of the hearing of 58 patients who had undergone our routine fenestration. He calibrated his audiometer daily against an artificial ear, and against an artificial mastoid by bone, and he ran all of the tests himself in the same quiet, sound-treated room in our office. He found an improvement in hearing by bone conduction almost identical with that found in Dr. Feldman's study, confirming the presence of the Carhart otosclerotic notch.

I also agree with Dr. Feldman's finding that the hearing in the ear not surgically treated does not improve after fenestration, provided the hearing tests are made carefully and the rather rare case of psychogenic overlay is recognized.

I question Dr. Feldman's final observations and conclusions. His measurements, made an average of 7.44 years after fenestration, showed no increase in nerve degeneration in either the operated or the unoperated ear, and from this he concludes that fenestration does not prevent nerve degeneration. I must submit that if his statistics are a true and accurate measure of the degree of nerve degeneration, then they indicate rather that fenestration prevents nerve degeneration in both the nonfenestrated and the fenestrated ear, for in 7.44 years we should expect a measurable increase in nerve deterioration in at least some of his patients, especially since some of them had reached the age of 65. I wonder how sure Dr. Feldman is that the bone units of his audiometer remained perfectly constant in their calibration during the ten years or so of his study. Despite the advantages of a very close association with Dr. Carhart and his audiology department, we have a constant problem in trying to keep a uniform calibration for our bone units. We do not feel that we can rely upon the bone curve *alone* in deciding whether or not nerve deterioration has increased in cases followed

for ten years or more. In the study made in 1951 by Adin and myself of 390 fenestrations followed for five to ten years after fenestration, we examined *both* the air curve and the bone curve in each case. As far as we could determine, in 71 per cent of 247 cases in which only one ear was fenestrated, neither the fenestrated ear nor the ear not surgically treated showed a significant increase in nerve degeneration. In 8 per cent both ears showed appreciable nerve deterioration, and in 21 per cent only one ear showed increased nerve degeneration. The surprising finding in our study was that when only one ear showed nerve deterioration, it occurred eight times oftener in the nonfenestrated ear.

I thought it would be interesting to study the series tested by McConnell with regard to further nerve deterioration in the seven years since he made his measurements. Of the 58 patients, 8 had the other ear fenestrated and 10 did not return later than one year postoperatively for testing, leaving 40 cases available for study. Each patient was carefully examined, using both the air curve and the bone curve to determine whether or not there had been a further cochlear loss. The results were as follows: in 23, or 57 per cent, of the fenestrated ears there was no further nerve deterioration; in 13, or 32 per cent, there was slight to moderate deterioration; and 4, or 10 per cent, were questionable. Of the ears not surgically treated, 15, or 37 per cent, showed no change, 23, or 57 per cent, showed slight to moderate deterioration, and 5 per cent were questionable. When nerve deterioration was confined to only one ear, it occurred five times oftener in the fenestrated than in the nonfenestrated ear. Thus, this rather small series seems to confirm the early study by Adin and myself, showing that fenestration apparently retards nerve deterioration in the fenestrated ear in some, but not in all, cases of otosclerosis. I should like to repeat what I said in 1955: "It is illogical to expect fenestration to have any influence on retarding nerve degeneration in otosclerosis, yet there is preliminary evidence to suggest that in some cases better cochlear function is maintained in the fenestrated ear than in the opposite unoperated ear."

It seems very clear that the last word has not yet been said on this important problem. I sincerely hope that a really careful study might be made of a sufficiently large series of a thousand or more cases followed for ten years or more after fenestration, to shed further light on this disputed subject. Such a study will certainly require the full-time services of a competent person or several persons over a period of months. With the audiometric records that are available on many thousands of fenestration operations, such a study can and should be made.

HALLOWELL DAVIS, M.D., St. Louis: Dr. Robert Bilger, of the Central Institute for the Deaf, has just completed an analysis of the follow-up tests of a group of patients fenestrated by Dr. Walsh some seven to ten years ago. The portion of his analysis that deals with the articulation scores of these patients is pertinent to Dr. Feldman's study, and I am indebted to Dr. Bilger and Dr. Walsh for permission to present to you the main results of this portion of Dr. Bilger's analysis.

Those of you who are acquainted with Dr. Walsh's views will not be surprised that it is not bone conduction that he has used as an indicator of cochlear reserve and of possible deterioration of the auditory nerve or sense organ, but articulation scores obtained with the PB lists as recorded by Rush Hughes.

The main question asked by Dr. Bilger is, "Does the relation between the articulation scores of the fenestrated and the unoperated ears of these patients change over a seven-year interval?"

First of all, Dr. Bilger found that the articulation scores of both sets of ears, those operated upon and those on which an operation was not made, fell off slightly between the third and seventh year. The lowering of the average articulation score at the seven-year period is statistically significant, but the point that interests us more is that there is no significant difference at any period between the fenestrated ear and the ear not operated upon. To the extent that these articulation scores and the Rush Hughes' recorded version of the PB lists are an indicator of the state of the end organ and associated neurostructures, there is no evidence, in this follow-up over a period of seven years, that the state of the end organ or of the nerve is influenced by the fenestration operation.

DR. FELDMAN: It is hard to disagree with people who agree with you.

Dr. Shambaugh, I agree certainly that the problem of calibration of bone conduction over a period of ten years is an insurmountable one. Clinically, it is an insurmountable one from one hour to the next. It is for this reason that we attempted to change the statistics a little by comparing the measures of the difference preoperatively between the ears and then the same measures postoperatively.

We made the assumption (it may be a

wrong one) that if the calibration was off ten years ago, it was off in the right ear and the left ear, or in the fenestrated and the unfenestrated ear. So we relied upon the difference between the ears as well as the difference preoperatively compared with the difference postoperatively. In order to study the question we had to start somewhere.

Second, another aspect of this study, not discussed here, may have led to some of my conclusions. I made a study of otosclerotics who had not been operated upon but who had a history of otosclerosis of variable duration. In that study, if we factored out age we could find no significant impairment of hearing by bone conduction. In other words, my conclusion is partly based on the fact that I don't know whether bone conduction really decreases because of otosclerosis as a general rule, but I would agree that this should be studied further. This is certainly no last answer and I would be very interested in seeing a similar study of a group of the so-called fulminating type. I think perhaps the findings would be different. Our sample was too small to study this group alone.

We also used articulation scores, Dr. Davis, and the results are not quite the same. The only group that separated and showed a poorer score was the failure group in terms of the fenestrated ear, which was not quite as good postoperatively.

AUDIOMETRIC MANIFESTATIONS OF INNER EAR PHYSIOLOGY: THE AURAL OVERLOAD TEST

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BY INVITATION

TODAY, with reconstructive surgery of the middle ear a dominant part of otology, adequate assessment of inner ear function is most important. There is no doubt but that some of the failures experienced by surgeons operating on the middle ear can be attributed to the unrecognized lack of sufficient cochlear reserve. This can occasionally be accounted for by the well established fact that middle ear lesions sometimes affect bone conduction measures in peculiar ways. Therefore, aside from establishing a spread between air and bone conduction thresholds, additional techniques of measuring the auditory response at sound levels above threshold have been deemed necessary. Thus we find speech and recruitment tests quite widely used. But speech tests present many difficulties, such as the native tongue of the patient and even his intelligence, and recruitment tests cannot always be carried out and are not very quantitative.

We have recently proposed a quantitative procedure called the Aural Overload Test, that purports to measure what in electronic terms would be called the dynamic range of the ear.[5] This test is based upon some of the known physiologic characteristics of the ear. A quarter-century analysis of inner ear function by means of the sound-induced electrical effects arising from the sensory cells of the organ of Corti has revealed phenomena which can be demonstrated audiometrically and are of value because this research has localized these phenomena in the inner ear. The Otosclerosis Study Group requested a report on the physiologic basis for this test and on the success experienced so far through its clinical use.

Preparation of this report was supported by the Research and Development Division, Office of The Surgeon General, Department of the Army, under contract no. DA-49-007-MD-634 and by the funds for research in Human Resources, University of Michigan.

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ANIMAL EXPERIMENTS

When the ear of an experimental animal is presented with a tone, an electrode placed anywhere in the vicinity of the cochlea picks up an alternating current wave that faithfully reproduces the wave shape of the stimulating tone. These potentials arise from the hair cells of the organ of Corti and are known best as the Wever-Bray effect.[17] If a pure tone is used as the source and kept at a low intensity level, the electrical response follows accurately any increases in intensity. If the sound pressure is doubled, the voltage (measured in microvolts) from the cochlea doubles. This is true up to a point; the response, when the sound pressure gets too high, no longer accurately follows the increases. When the sound pressure in–voltage out curve is plotted there is no longer a straight line at these levels and one can see that the limit of linearity has been reached. As the stimulating sound pressure is increased further, a maximum in response is approached and beyond the maximum there is a decrease. If the tone

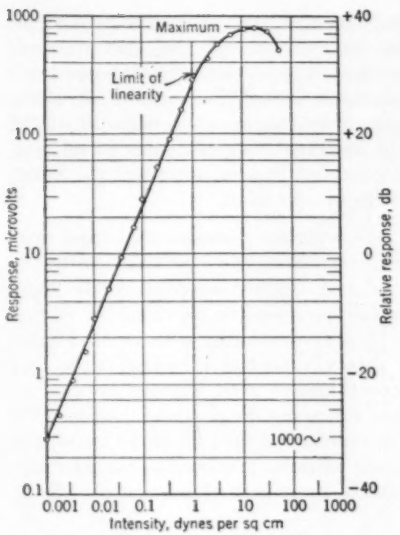

FIG. 1—Intensity function as recorded by measuring the electrical response of the cochlea to a tone of 1000 cps. 1 dyne/cm.^{2} = 74 db above .0002 dyne/cm.^{2} (From Wever and Lawrence.[21])

remains at this high level, or is further increased, damage to the inner ear sensory structures will inevitably follow.

Figure 1 shows the response curve to a tone of 1000 cycles per second (cps). The limit of linearity and the maximum point are indicated. Similar curves can be recorded for all audible frequencies even though there may be differences in sensitivity. Such differences show up as a shifting of the curve to the left or right depending upon whether the ear is more or less sensitive. A shift to the right, for example, would indicate that more sound pressure is required to produce a certain voltage output.

For this electrical response there is no threshold such as is known in audiometry; the lower measures are limited only by the physiologic noise level of the animal, or the vacuum tube and thermal noise level of the recording equipment. As the stimulating tone is made more intense, the response increases in the same amount and proceeds to do so until the limit of linearity is reached. Frequencies below 1000 cps reach approximately equal maximums, but the magnitude of this measure decreases rather uniformly as the frequency is increased.[20] For our purposes here, the next consideration is which of the auditory structures is responsible for limiting the response in this manner. One might suspect, since sound pressures that produce a maximum response give rise to injury of the inner ear only, that it is the inner ear that is limiting the response, and numerous experiments have shown that this is true.[21]

It is really quite astounding to find how truly linear the middle ear is in its response to sounds of increasing intensity. An electrode on the cochlea reflects the properties of all the peripheral structures up to and including the source of the recorded potentials, and anything that impedes the transmission of acoustic vibrations along the aural pathways lessens the amount of cochlear alternating current voltage for a given sound pressure. But this is merely a loss in sensitivity, a conductive deafness. If the sound level is raised sufficiently to vibrate the inner ear structures, the limit of linearity is seen to occur at the original response level. Within a very small amount of variation, this is true under any sound conduction impairment of the middle ear. The drum membrane can be perforated, the middle ear air pressure increased or decreased, the ossicular chain disarticulated or, as will be shown shortly, the stapes can be ankylosed or the middle ear cavity filled with adhesions or suppurative material, and the response level of the limit of linearity remains approximately the same.

A most striking bit of evidence comes from experiments in which the drum membrane and ossicles, except for the stapes, are removed entirely.[18,21] Figure 2 shows the response curves under the

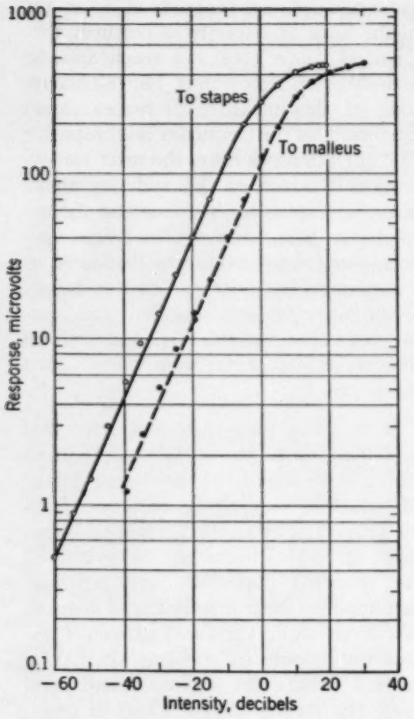

FIG. 2—Intensity function for 1000 cps recorded when first the malleus and then the stapes is driven by a mechanical vibrator. (From Wever and Lawrence.[21])

two conditions. In this experiment a needle driven by a crystal vibrator was first placed on the umbo of the malleus and a sound pressure in–voltage out curve recorded. The drum membrane and ossicles were then removed and the vibrating needle placed on the head of the stapes. Because the lever ratio of the ossicular chain is now lost, the amplitude of vibration on the stapes is greater by the amount of the lever ratio (about 2.5 to 1 in the cat) than it was after traversing the ossicular chain. So we see that the response for a given sound pressure is larger when a given amplitude is applied to the stapes than when it is applied to the malleus. The magnitude of the response shows what is going on at the hair cells and, as these curves show, the limit of linearity and maximum are reached at approximately the same level. Manipulation of the middle ear structures may change the sensitivity of the ear by interfering with the sound conduction but it does not affect the linear range of operation.

If anything disturbs the inner ear, however, an entirely different picture is produced. Such conditions can be most readily produced by death of the animal or by overstimulating with sound. Figure 3 shows a normal response curve and several others after various periods of time following the death of the animal.[19] The numbers at the tops of the curves indicate minutes following the last detectable heart beat of the animal. Under

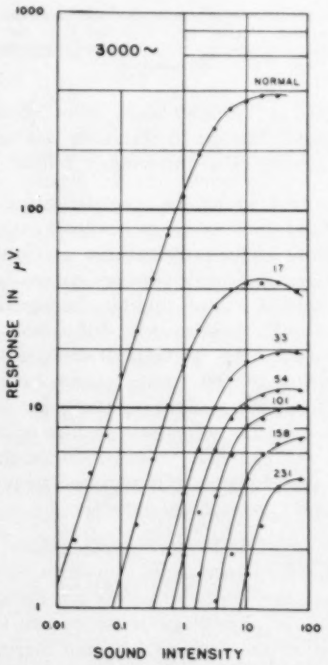

FIG. 3—Intensity function for 3000 cps before and following death of the animal. The numbers at the maximums of the curves indicate minutes after death. (From Wever, Bray and Lawrence.[19])

these conditions not only is sensitivity lost, as indicated by shifting of the curves to the right, but also the response levels of the limit of linearity and maximum response are lowered. The dynamic range of the ear is thus seriously affected.

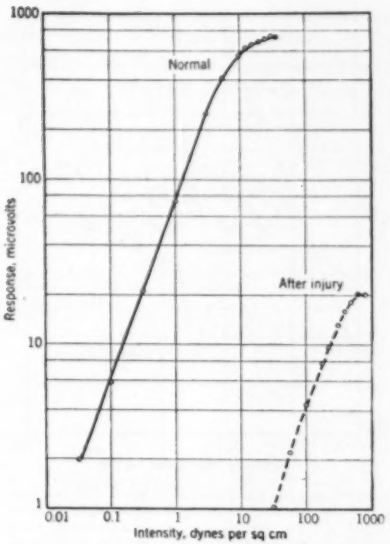

FIG. 4—Intensity function for 300 cps before and following overstimulation with 700 cps. (From Wever and Lawrence.[22])

The same picture is produced after damage to the inner ear of the animal by the introduction of excessively intense sounds.[22] Figure 4 shows a normal response curve and a curve made after severe acoustic injury. Again, not only has sensitivity been lost, but the dynamic range has been drastically decreased.

On the basis of this evidence and considerably more it is apparent that the linear range of operation of the auditory structure is determined by the inner ear. It is true that the middle ear will become nonlinear if driven by excessive amplitudes, but such conditions would have already destroyed the inner ear.

It must be clearly understood that there are several explanations of how this limiting takes place in the inner ear and that there are several structures that could be responsible.[1,3,16] Our specific concern here is to show that departure from linearity is a property of the inner ear, not the middle ear, and that only changes in inner ear conditions affect this linear range.

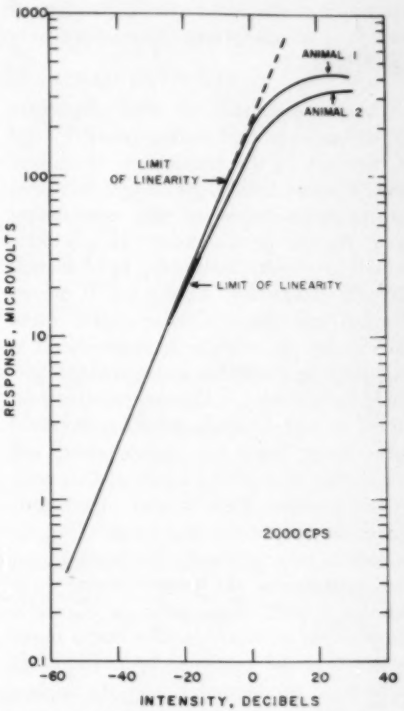

FIG. 5—Intensity function in response to a tone of 2000 cps to show individual differences in limit of linearity and maximums even though sensitivities to low level sounds remain the same. (Adapted from Lawrence and Blanchard.[8])

Since the linear range is so dependent upon inner ear conditions, one would expect to find individual differences in this dimension. Figure 5 shows that such differences do exist even when sensitivi-

ties remain the same.[5] These curves are for two guinea pigs stimulated with the same frequency. At low sound pressures the two responses coincide, but one departs from linearity and reaches a maximum at a lower intensity and response level than the other. This suggests the possibility that if the linear range of operation could be determined audiometrically in the human ear, there would be a means of determining the physiologic condition of the inner ear independent of middle ear alterations that affect only sensitivity.

A characteristic of this departure from linearity that makes possible such a measure in the human ear is that as the response fails to give equal increases to intensity raises of the stimulating tone, the ear produces harmonics, tones which are multiples of the fundamental driving frequency. As the ear is driven further into the nonlinear region these harmonics rise rapidly in intensity. It is possible, again in an experimental animal, by use of a voltmeter that can be tuned to any desired frequency, to measure these harmonic components and show that they exist as part of this nonlinear process. This is also called nonlinear or amplitude distortion. The ear is said to be acoustically overloaded, and the occurrence of rapidly rising harmonics is part of the process. Figure 6 shows such an analysis. The curve numbered 1 is the response to a 1000 cps pure tone fundamental, and the higher numbered curves show the rapidly rising harmonics: curve 2 is the 2000 cps harmonic; curve 3, the 3000 cps, etc. Of course it is absolutely necessary in this type of experiment that the stimulating tone be as free from harmonics as is technically possible so that the distortion products present in the electrical response are known with certainty to arise in the ear.

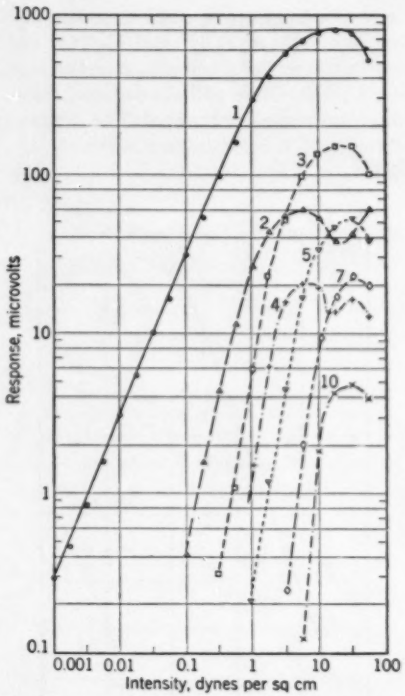

FIG. 6—Intensity functions for a pure 1000 cps tone and for the harmonics arising from within the inner ear. The number appearing at the maximum of each curve designates its order in the harmonic series; e.g., number 2 represents the 2000 cps component. (From Wever and Lawrence.[21])

CLINICAL EXPERIMENTS

It has been known for some time that these aural harmonics can be heard by a human observer, but they were never dealt with experimentally until Wegel and Lane[15] of the Bell Telephone Laboratories introduced the exploring tone technique in their 1924 article on masking. To determine the limit of linearity, or the point of onset of overload, in the human ear, it is only necessary to find the level of a pure stimulating tone at which the harmonics can just be detected. To do this, the exploring tone method of Wegel and Lane can be employed (fig. 7).

A filtered, pure tone of, say, 1000 cps whose harmonic content is known to be less than 0.1 per cent is delivered to the ear. At low levels, only this tone is heard. As the intensity is raised, an experienced listener may detect the presence of harmonics in the tone he hears. Since these overtones are difficult to hear, a second exploring tone, the frequency of which is only a few cycles per second different than that of the second harmonic, is introduced. This second tone beats with the aural harmonic and these beats can be heard in the background of the fundamental. Best beats occur when the intensities of the beating tones are equivalent,[6] and since the aural harmonic is weaker than the fundamental, the exploring tone must be kept less intense than the overloading fundamental. By increasing or decreasing the intensity of the fundamental and then varying the intensity of the exploring tone until best beats are heard between it and the aural harmonic, it is possible to determine the equivalent intensity of the aural harmonic by determining the intensity of the exploring tone. In this way the growth of the aural harmonic, as the ear is driven further and further into the overloaded region, can be traced,[6] and the resulting curves bear a marked resemblance to those recorded in the analyzed electrical response from the cochlea of an experimental animal. It is also possible, by the same method, to determine the intensity level of the fundamental at which overloading, or the onset of nonlinearity, is reached. When the fundamental is below the level of overload two tones can be heard: the fundamental and a weaker exploring tone. At the point of overload, or higher, the fundamental and a weaker, beating tone are heard.

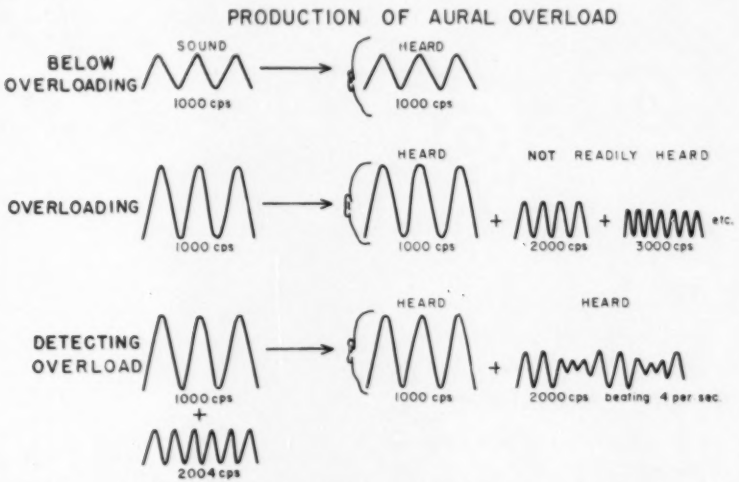

FIG. 7—The method of detecting harmonics in the human ear. At low levels when the ear is stimulated with a pure 1000 cps tone, only that tone is heard. At high levels the ear overloads and produces harmonics which are present along with the fundamental. To aid in the detection of these harmonics, an exploring tone is introduced which then beats with the aural harmonic and is heard in the background of the fundamental.

It should be pointed out that ever since the exploring-tone method was first employed, there have been several objec-

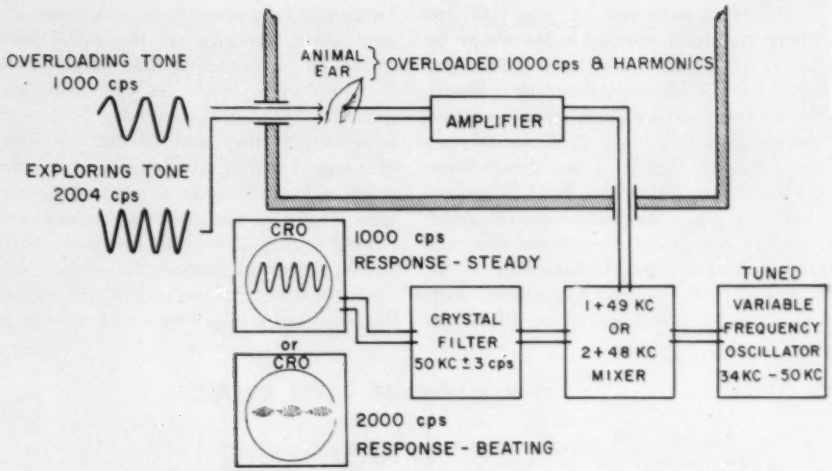

FIG. 8—Equipment arrangement in an experiment to determine whether an exploring tone (2004 cps) modulates the fundamental (1000 cps) through interaction within the inner ear. The response to the fundamental, or harmonic, can be separated by having them combine with either 49 kilocycles or 48 kilocycles respectively from a tuned variable frequency oscillator and passing the resulting 50 kilocycles through a crystal filter. This is done within a G. R. type 736-A wave analyzer. The result is portrayed on a cathode ray screen. At low levels two pure tones are recorded in the response, which is the way the ear hears them, but when overloading is reached and the aural harmonic arises, the response to the exploring tone alone is seen to beat. It is necessary to remember that the ear itself acts like a frequency selective filter in which components of a complex tone can be heard out (Ohm's law). This immediately makes it improper to think that the hearing process is like a nonselective circuit that consists of mixing and interaction of any and all components, as supposed by critics of the exploring tone technique (see text).

tions to this technique. Max Meyer[11] in numerous articles has vehemently denied the existence of aural harmonics. Trimmer and Firestone,[14] and more recently Chocholle and Legouix,[2] have expressed the notion that any mistuned octave will interact with the fundamental to give beats, making the method inadequate for the detection of aural harmonics. And Békésy,[1] using the same argument based on experimental work with his skin-vibrator model of the cochlea, while admitting the clinical value of the method, denies that the beats are between an aural harmonic and the exploring tone. There is, however, considerable evidence that indicates the validity of the technique[8]:

a. Experienced observers, without the aid of an exploring tone, can hear the harmonics and they appear at the same intensity level of the fundamental as they do when heard with the aid of the auxiliary tone.

b. Below the level of overload two distinct nonbeating tones can be heard: the fundamental tone and the exploring tone. If the ear were like Békésy's model, a beating tone should be heard all the way down to the threshold of the fundamental.

c. Lewis and Larsen[10] have shown that when the ear is overloaded the harmonic will be heard to interact with an exploring tone of exactly the same frequency as the harmonic but shifted in phase. This would not occur if there were no harmonic, since the fundamental is heard to remain constant.

d. It is possible at some frequencies to introduce the exploring tone into the op-

posite ear and experience a binaural beat between it and the harmonic arising in the overloaded ear.

e. By introducing an exploring tone into an animal's ear which is overloaded with a pure tone, it is possible to use a frequency selective voltmeter to determine whether there is any interaction between these two tones. Figure 8 shows the arrangement of equipment for performing this experiment. An overloading fundamental is directed into the animal's ear and the strength of the second harmonic read by means of the voltmeter. This fundamental is turned off and a second tone a few cycles per second different than the harmonic is presented and adjusted to give the same response on the voltmeter that the harmonic gave. The overloading fundamental and the exploring tone are then turned on together and the selective voltmeter tuned to the harmonic frequency. It is seen to beat at a rate equal to the frequency difference between the harmonic and the exploring tone. When the voltmeter is tuned to the fundamental, no appreciable disturbance is observed. This clearly indicates that, at least up to the point at which these electrical potentials are generated, there is no interaction between the fundamental and the exploring tone and that an aural harmonic has to be present to produce the beats. In view of this evidence the exploring tone method as a valid technique for detecting conditions of overload in the inner ear of the human appears reasonable.

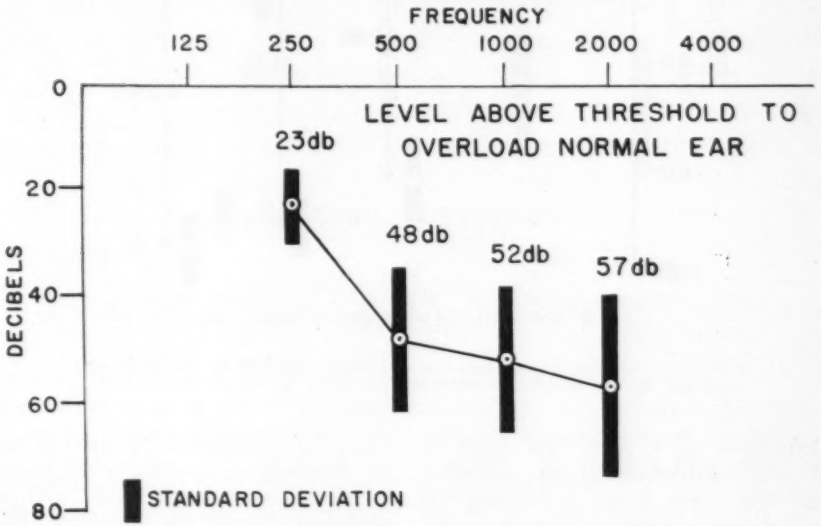

FIG. 9—Thresholds of aural overload in normal ears. Each point represents the level above audibility threshold to which the designated frequency must be raised to produce just noticeable overloading.

By using a number of observers with thresholds within normal limits it is possible to find the average dynamic range of the ear for various frequencies and determine the extent of its variations. Fletcher[4] published a curve showing the level above threshold at which various

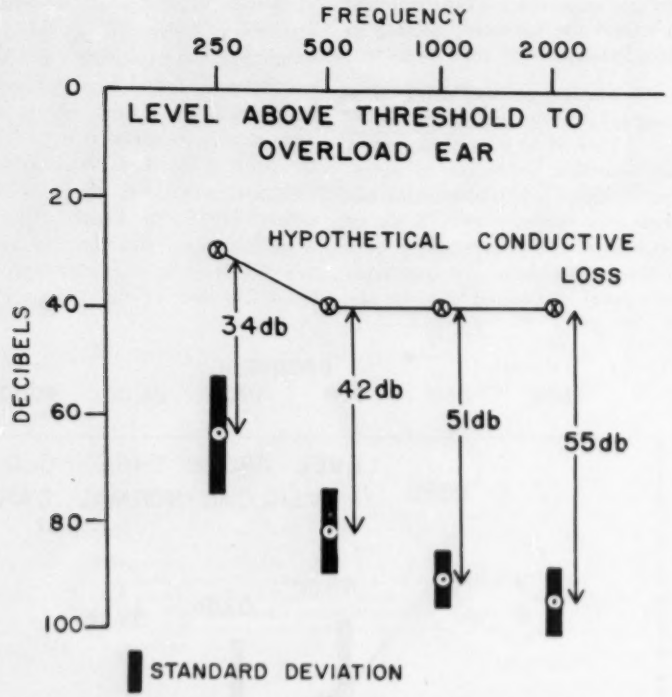

FIG. 10—Thresholds of aural overload in ears with a conductive loss. The linear range is almost identical with that of normal ears.

harmonics of a pure tone could be heard, but no determination of individual differences was shown. Advocating that this technique could be clinically useful, Lawrence and Blanchard[5] carried out a series of experiments in a specific effort to determine the amount of variation in onset of overload among normal hearing individuals, but the number of observers was small. Later, larger groups were employed for 1000 cps and 2000 cps, and these data[7] have been used in conjunction with the earlier data for the illustration here. Figure 9 shows, in audiogram fashion, the lowest levels above threshold to which each of four frequencies must be raised to produce, in the background of the fundamental, the audible beats between aural harmonic and exploring tone. The area between the zero line and the threshold of overload is the region in which sounds can be heard with no distortion. Beyond the lower line, distortion products can be heard. The reason these overtones are not noticed in everyday life is that the listener is never subjected to pure tones. Every bit of music and human voice is richly filled with harmonics which mask out any aural overtones that might be present.

The mean threshold of overload for this limited number of subjects occurs at 23 db above audibility threshold for 250 cps, 48 db for 500 cps, 52 db for 1000 cps, and 57 db for 2000 cps. The standard deviations of these measures are shown so that they can be used as a standard in estimating whether a patient

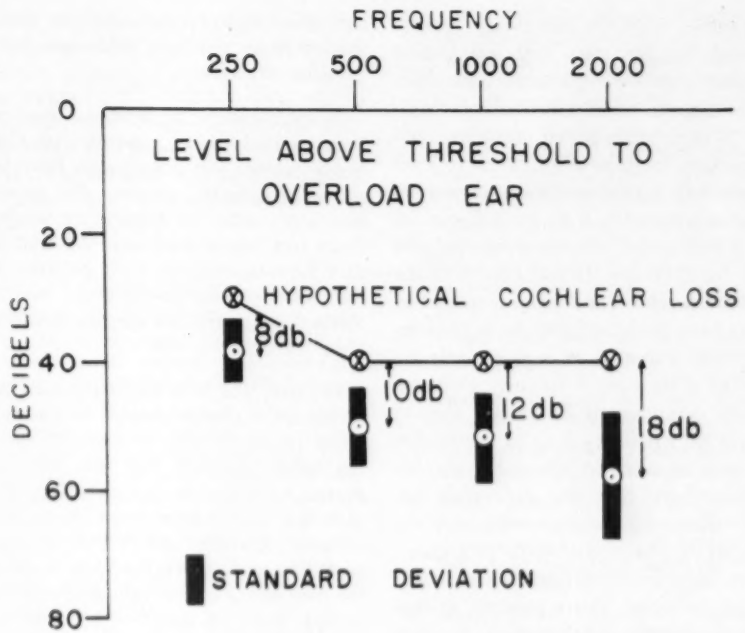

FIG. 11—Thresholds of aural overload in ears with a loss in hearing attributable to inner ear disease. The linear range is markedly restricted.

has a normal or an abnormal overload level. The actual range of overload thresholds in normal observers extends considerably beyond the limits of the standard deviation. Both 1000 cps and 2000 cps show overload levels ranging from 5 db above threshold up to 80 db for various observers.

Overload measures that have been carried out on patients with conductive losses show ranges of linear operation of the ear almost identical to those of the observers with normal hearing, but the patients with hearing losses attributable to inner ear lesions show a marked restriction of this linear range. The clinical data presented here are from Opheim and Flottorp[12] for 250 cps and 500 cps and from Lawrence and Yantis[7] for 1000 cps and 2000 cps. Figure 10 shows a typical conductive loss thresho'd curve and below it the mean level of overload for the four frequencies. From audibility threshold to point of overload the linear range is practically identical to that for the normal ear. The middle ear impediment (otosclerosis and chronic otitis) has merely necessitated shifting the sound level higher but has not appreciably changed the overloading characteristics of the ear as a whole. This observation in itself is supporting evidence that the middle ear is not involved in the aural distortion process even when affected by disease.

In contrast with these results, inner ear disease has a very marked effect upon the level at which the ear overloads. This, of course, was predicted from the results of the animal studies and shows up clearly in figure 11. The data from which this figure was made

were taken from the same two reports as those for the ears with conductive loss and represent patients with Ménière's disease, neomycin toxicity, childhood fevers, stimulation deafness and presbycusis. In these cases the mean level of overload above audibility threshold has been reduced to 8 db for 250 cps, 10 db for 500 cps, 12 db for 1000 cps, and 18 db for 2000 cps. In addition, both the standard deviation and general spread of results have been reduced. It is obvious why, with a dynamic range of only 10 to 18 db in the speech frequencies, these patients complain of not being able to understand what they hear or are unable to wear a hearing aid. There are also indications here that the difference between the audibility threshold and the overload threshold may serve as a quantitative measure of the severity of cochlear involvement. Many patients in this category experience distortion as soon as a tone is heard, i.e., the threshold tone contains aural harmonics. In others this may not occur until the tone is 5, 10 or 15 db above threshold. Since the normal ear does not overload until around 50 db, there is considerable possibility for a quantitative interpretation.

As has been observed in the animal experiments described earlier, inner ear disease not only lowers the response level at which overloading starts but it seems also to bring it on quite rapidly. That is, once the overload level has been reached, the harmonics produced grow very rapidly. So it is not surprising that patients with cochlear deafness have less trouble hearing the beating harmonics than do other observers. Once overloading sets in, the harmonics begin to dominate the experience. It has also been a common observation that, in cases where it can be measured, recruitment invariably exists along with the lowered overload threshold. Sokølowski[13] and Opheim and Flottorp[1,2] recommend the use of the overload test as a substitute for recruitment tests.

Some measures of overload level have been carried out on patients with eighth nerve tumors but not enough have been made to indicate whether the measure has any value in separating cochlear from true nerve deafness. Without further investigation on such patients it is difficult to predict just how the inner ear distortions would be perceived through a damaged nerve.

Because the overload threshold level seems to be closely related to the maximum response and subsequent injury, the aural overload test was first suggested as a means for detecting those ears that might be susceptible to noise-induced hearing loss.[5] The objection raised to such a proposal has been that the idea had not been validated in human beings. Since no such test has ever been truly validated, this is certainly as legitimate a criticism for the overload test as it is for the others, but the test for distortion in the ear does seem to have the advantage that the process is known to be related to actions of the structures of the organ of Corti, the locus of damage by loud sounds. Distortion thresholds are also known to be lowered by brief stimulation of loud tones.[9] Validation programs are in progress at the present time, and the usefulness of the overload test as a measure of susceptibility should some day be known.

Many interesting theoretical implications of these distortion characteristics of the inner ear exist. The exact source or method of production is not clearly understood, and the peculiar nature of its behavior in pathological conditions of the inner ear needs a great deal of investigation. For example, if hydrops is present in Ménière's disease, it must be as a phenomenon accompanying others that affect hearing in serious ways, be-

cause it is difficult to explain a limited linear range solely on the basis of a fluid pressure change. Further use of the aural overload test will not only add to the certainty of diagnosis but will furnish additional data on inner ear diseases, data that may help in determining the causation of what are now incurable forms of deafness.

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DISCUSSION

THEODORE E. WALSH, M.D., St. Louis: Dr. Lawrence has presented another test designed to assess cochlear dysfunction. He has presented very clearly the method of testing and the experimental evidence for the test. There are some points I want to discuss and some questions I want to ask.

First, I wonder if the aural overload test is really going to be helpful in assessing the

degree of cochlear dysfunction in mixed deafness. In his opening paragraph Dr. Lawrence indicates that it will. Yet in his report in the Archives of Otolaryngology in January 1956, he reports several cases of so-called mixed deafness which I wish he would explain. The range from threshold to overload in middle ear disease has a mean of 51 decibels and a standard deviation of 5 for the 1000 cycle tone, and a mean of 55 decibels and a standard deviation of 6 for the 2000 cycle tone. Does an ear with a threshold to overload range for the 1000 cycle tone of 45 or 50 decibels have cochlear dysfunction? And if so, how much? Is this really a mixed deafness or a pure conductive deafness? Surely it is much easier to estimate by the use of speech tests whether one can help this patient surgically. If the patient's discrimination score is such that he would be made socially adequate by improvement of his threshold for speech, then the operation is worth while. If his discrimination score is too poor for him to be socially adequate how ever much his threshold is improved, surely the operation is contraindicated. I doubt that the aural overload test will be of much help to those of us who are doing surgical procedures on the middle ear.

I want to ask Dr. Lawrence about his experience in the test-retest reliability of the aural overload test, and, further, I should like to know how difficult it is for the patient. I tried it the other day myself and found it quite difficult.

This test might be helpful in the differential diagnosis between cochlear lesions and those central to the cochlea, specifically between Ménière's disease and cerebellopontine angle lesions. A differential diagnosis is not always easy to make in these conditions, and the hearing studies are frequently hard to assess. This test should give us information if it actually differentiates end organ lesions from central lesions. Apparently, there are still too few cases of central lesions studied to make the results statistically significant.

I expect that this test may be helpful in assessing which ears are particularly susceptible to noise, and it might be an excellent screening tool for employment in noisy industry. I suppose that those normal patients who have a range from threshold to overload in the low values, for example 30 decibels or less, should not be given employment where there is excessive noise. These ears are probably more liable to acoustic trauma than are those with a large range.

If I understood him correctly, Dr. Lawrence feels that bone conduction audiometry is not always diagnostically reliable. I agree with him. I congratulate him on producing another test which will be a check in regard to this very important matter. For example, I wonder how the patient who was sent to me for a possible operation on the middle ear, with a tentative diagnosis of otosclerosis, would have come out with the aural overload test. He had a positive Rinne in spite of having excellent discrimination in both ears. I believe the diagnosis to be perceptive deafness, but I have seen patients with early otosclerosis who do show a positive Rinne; I am sure all of you have. This aural overload test might very well be utilized to help us in making a differential diagnosis.

I agree that bone conduction curves can do strange things in cases of middle ear disease. For example, we have several patients on whom the bone conduction curve has completely changed after stapes mobilization. The aural overload test in this instance might have given us some information, although tuning forks and speech tests helped us determine whether or not to operate.

Dr. Lawrence is to be congratulated on this paper and on presenting us with a new test of cochlear dysfunction. I would like to emphasize that this is an added test which, when used intelligently and correlated with other hearing tests also used intelligently, will help to make a diagnosis of hearing loss. I am sure Dr. Lawrence agrees that a great deal of work remains to be done before the full significance of the test can be evaluated. Until this research has been done, I hope that the manufacturers of audiometers will not add apparatus for doing aural overload tests to their clinical audiometers.

CLAIR M. KOS, M.D., Iowa City, Iowa: Anyone familiar with the complexities of hearing loss will agree that an accurate assessment of hearing acuity is not always a simple task. Often it becomes a time-consuming chore and, unless devotion to accuracy and understanding in certain instances is intensified, therapeutic errors of commission and omission are bound to arise.

Obviously, the conventional air and bone conduction tests have their limitations, but their usefulness has been augmented by more complicated measurements of the impedance of tympanic structures, speech discrimination, temporary threshold shift, PGSR audiometry, a confusing battery of recruitment tests, and now, possibly, a test for aural overload.

Fortunately, an adequate history, physical examination and the fundamental tests of air and bone conduction sensitivity still serve to

indicate a clinically practical and useful diagnosis of the majority of ear diseases. Unfortunately, the cost, space requirements, operational difficulties and time required to administer the more exploratory tests make it too inconvenient, if not impossible, for the otologist to perform them. Consequently, most of these special tests are available only to otologists who employ competent audiologists or those who command audiologic services in teaching and research institutions.

I must emphasize that if the air and bone conduction sensitivity tests are conducted properly under the protection of reasonably controlled conditions, and if surgeons operating on the middle ear would conscientiously pause long enough to ascertain the true capacity of hearing by these methods before rushing into a possible surgical solution, the failures mentioned by Dr. Lawrence would be reduced considerably.

The provocative potentialities of the aural overload test are stimulating to the imagination. It is a fascinating phenomenon to experience. It is not difficult to administer—if you have the equipment to deliver the appropriate stimuli.

The test results at this stage of development may not be as easily defined as the author suggests. Since the test itself seems to initiate a chain reaction by the production of aural harmonics, evidence of functional activity is multiplied to the extent that additional features of the response are made available for study.

A fundamental tone is introduced at a given intensity. Then another tone four cycles above the first aural harmonic is added. This second tone is the exploratory tone—searching, by varying the intensity, the sensation level at which beats are heard best. This plateau represents the threshold of overload for the fundamental tone selected.

According to this study, the mean threshold of aural overload in normal and tympanically impaired ears is approximately 50 decibels above the threshold of audibility. However, the overload levels range from 5 decibels to 80 decibels among the subjects tested. As a clinician I must admit to some confusion concerning the quantitative significance of a procedure which exhibits as great a range of individual differences as is characteristic of the aural overload test. Perhaps it is this marked variability of individual differences in intensity levels required to overload the ear which suggests the possibility of its use for the detection of noise susceptibility. If so, I am concerned about the hearing of the observer whose overload threshold developed at 5 decibels above audibility.

I interpret these conclusions to mean that as much variability is to be anticipated in the sensation levels at which overloading occurs in ears with tympanic disease as in normal ears, since it has been shown that the tympanic structures have little or nothing to do with the generation of aural harmonics. If this is correct, it follows that this rather large overload variability reduces the accuracy or significance of quantitative evaluation of the cochlear reserve in patients with tympanic or combined tympanic and cochlear diseases.

The data presented do not show that this variability is eliminated by cochlear or neural involvement, although it is interesting that the linear dynamic range is reduced in ears with cochlear disease. This more significant observation suggests that the overload test may lead to more effective techniques for differentiating between different areas of inner ear involvement, provided individual differences at which aural overloading occurs are not extreme.

The standard deviations of the sensation levels at which overloading occurred in ears with otosclerosis were considerably smaller than the comparable standard deviations in cochlear disease. Since the linear dynamic range is less in ears with cochlear disease, one would expect to find the standard deviation smaller—but such is not the case. Perhaps Dr. Lawrence will comment on this further.

At this point I am not convinced that the overload test is a more accurate quantitative test for recruitment than the presently available direct measures, but I intend to subject some of my patients to this test to learn more about it.

As Dr. Lawrence has stated, much more information is needed to establish the diagnostic value of this test; also, there is a need for standardization of terminology concerned with physiology, technique, and statistical treatment of the test.

I congratulate Dr. Lawrence for his pioneer work with this procedure.

HALLOWELL DAVIS, M.D., St. Louis: The topic of this paper is very close to my heart, because in our own laboratory we have observed many of the phenomena that Dr. Lawrence has described in regard to the electrical output from the ear of the cat. We, too, have observed and have been studying the phenome-

na of nonlinearity about which he has spoken. Notice that I use the word "nonlinearity" and not the word "overload."

My first comment is that I am afraid that the word "overload," although it is technically correct from the point of view of mechanics to designate exactly this departure from nonlinearity, gives an impression of physiological stress and danger that is entirely unjustified. I call attention to the fact that the point of nonlinearity in Dr. Lawrence's chart of the input-output curve of the cochlear microphonics occurs at about the middle of the physiologic range, that is, about at the level of conversational speech. We have confirmed this observation many times, and I think it is ridiculous to be worried about overload at this level as a threat, a stress, or a danger. I propose a different line of interpretation, which will give us almost the same results as Dr. Lawrence obtained. We can regard this appearance of nonlinearity as the manifestation of a protective mechanism in the inner ear which prevents the very sensitive external hair cells from being overstressed or these hairs distorted too far by the very wide dynamic range of sounds to which they are subjected. When this protective mechanism comes into action, another set of receptors of higher threshold takes over and thereby extends the range of sensitivity of the ear. There is no doubt, however, that we do have harmonic distortion. An oscillogram shows the suppression of the peaks. If we put the electrodes in a different position in the cochlea, the wave form is quite different but nevertheless distorted.

I agree completely that we have distortions and aural harmonics. They are real, but I believe they are physiologic. The ear is accustomed to dealing with peak-limited waves. We get them physiologically and we get them from many of our communication systems, and as far as communication is concerned, the ear tolerates this kind of distortion extremely well. Peak clipping must be very extreme to destroy intelligibility even though the quality deteriorates and things sound harsh and tinny.

I believe that it is in the ability of the ear to do a job of discrimination and synthesis that the real failure occurs in abnormal ears. It is not that nonlinearity is more or less, but that the ability of the ear to deal with the distortion products is not good.

Now, with this point of view, it is still legitimate to use the threshold of detection of harmonics to test for abnormality. I think it is very significant that the threshold is more precise, with a smaller standard deviation, and that the whole phenomenon is very prominent in tests on abnormal subjects. The normal ear, apparently, can bypass the distortion, suppress it and hear around it, as it were, while the distortion stands out and makes trouble for the ear that is not entirely normal.

Normal subjects apparently differ widely in their ability to hear the beats, but if the abnormal subjects do hear them more easily, the beats are the basis of something useful.

We don't need more tests; we need better tests. It is only by clinical experience and the kind of trial that Dr. Kos said he is going to make that we can arrive at any real evaluation and see what it is that this new method offers us.

DR. LAWRENCE: The discussers have indeed hit upon the essential problems involved in this new procedure, and in the initial presentation I think I alluded to some of them as well as other difficulties. It is not possible to comment on all the items in the length of time remaining, so I would like, briefly, to cover only a few, commenting upon the remarks of Dr. Davis first.

Dr. Davis observed that our understanding of the physiology underlying this test is incomplete, which serves to emphasize the statement I made, that a thorough analysis of the cochlear action involved in the distortion process has not yet been carried out and will involve considerably more investigation. Since we are agreed on this, there is no need to discuss the problem further: it remains for future research.

As to the question of the semantics of the word "overload," there may be no need to worry about it. If the procedure proves to be universally practical, the term will be understood; if it does not, the question of its use is academic.

Dr. Kos mentioned individual differences. He called attention to the fact that the standard deviation seems to be a little greater in the cases of inner ear involvement. This may be due to the limited number of cases reported, which, as a matter of fact, may have affected all the statistics shown. The important thing is that there is a marked difference between the linear range of hearing in those individuals with a conductive loss and that found in those with involvement of the inner ear.

The extent of the standard deviation in patients with involvement of the inner ear may, however, be related to the question raised by Dr. Walsh. This concerned the possibility of the procedure having a quantitative value, in that there is a linear range of from 50 de-

cibels to no range at all: overloading occurring at threshold. There does seem to be some indication that if the range is restricted, the amount of restriction expresses the severity of the involvement of the inner ear, but this interpretation requires the amassing of considerably more data.

In the case of a mixed deafness the suggested procedure seems to have its greatest value in that it is possible to reveal inner ear involvement in the face of quite severe conductive loss, and so cautions the otologist contemplating surgical procedures.

Dr. Kos also mentioned the fact that the normal ear showed a range of from 5 to 80 decibels. The distribution tails off considerably at this lower end, and in all the measurements we have made we have had only one individual with normal hearing and a linear range of only 5 decibels. Similar measures that have been made in industrial concerns have also shown an extensive spread but, here again, those with shortened linear ranges become fewer in number the shorter the range.

I will give a quick answer to the question about test-retest reliability. This is a fairly difficult procedure to carry out. It takes considerable practice in maneuvering the exploring tone in that it involves an understanding of how these harmonics grow in the ear as it is driven further into the region of nonlinearity. One of the industrial concerns that has employed the procedure has reported privately that they used five different operators to give the test to several individuals before they proceeded with an over-all study. At each frequency employed, the results agreed within 5 decibels. In view of the difficulties of giving the test, this is rather remarkable, but apparently the test is reliable if the technique involved is understood.

We have little information on the characteristics of the linear range of hearing in the presence of an acoustic nerve tumor. It is difficult to interpret just how these responses of a normal or abnormal inner ear would be perceived through a damaged nerve.

One last comment related to the statement that there need be no supplementary test for the comparison of bone and air conduction if these latter measures are properly performed and interpreted. If it is possible accurately to determine the extent of the cochlear reserve by means of bone conduction, air conduction and speech discrimination tests, then we ought to have no more complaints from surgeons who operate on the middle ear that lack of success is due to some undetected inner ear involvement.

I wish to thank the discussers for their thoughtful consideration of the data presented here.

THE USEFULNESS OF THE BINAURAL HEARING AID

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BY INVITATION

THE development of ultraminiature hearing aids has greatly increased the practicality of specifying their binaural use. The clinician must, in consequence, be alert to the advantages and limitations of the binaural system. He must have clearly defined criteria for the hard-of-hearing patient.

A wearable binaural device employs two complete hearing aids, one for each ear. Since the sound patterns striking the microphones of the two hearing aids are not identical, the sequence of excitatory events reaching one ear is not only independent of but also different from the sequence reaching the other ear. It is this fact which gives the binaural system its potential for sharp superiority over either a monaural system or an arrangement by which one amplifier supplies stimuli to both ears.

To explain: The world of sound assumes full three dimensionality only when the capacity for spatial localization can be used to its fullest. Normal ability to distinguish sounds of biological and social importance in unfavorable listening situations requires that two independent sequences of neural events, one from each inner ear, activate the central nervous system. Under such circumstances sources of sound are more effectively localized than when a single train of neural events is present or when the two trains are identical. When independent sequences of neural events are present, the listener can distinguish more effectively among competing sounds arising from different points in his environment. This capacity allows him to hold his attention on the stimuli which are at the moment important even though the situation is, acoustically, quite chaotic. To restate in the language of the psychologist: foreground and background relationships can be more effectively crystallized when three dimensionality is preserved in the auditory environment.

As viewed by the physicist, the capacity to localize sound depends on the fact that the two ears are separated by the head. In consequence, the listener achieves an auditory triangulation on every source of sound. The specifics of this triangulation vary precisely with the location of the source in relation to the listener. The situation is illustrated schematically in figure 1. The two ears will receive identical acoustical excitation only when the source is in the midline sagittal plane, as exemplified by position A in the figure. Any other location of the source, for example, position B, produces bilaterally dissimilar acoustic excitation because the paths to the two ears are no longer the same. Physically, the two stimuli must now be different in one or more of the following dimensions: (1) *intensity*, which will be affected by the distance from the source and the diffraction effect of the head; (2) *time of arrival (phase)*, which will depend on relative distance from the source; and (3) *spectral composition*, which will be determined by the diffraction effects of the head.

Experimental psychology has long since demonstrated the relationships

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which exist between the physical dimensions of a pure tone and the precision with which the source of this tone can be identified.[4] The rules for localization of complex sound and the role of localization in everyday listening are less fully defined by precise research. However, the contribution of binaural reception to ordinary adjustment is clearly apparent to the alert observer. Koenig,[1] for example, reported after he controlled listening situations systematically that a hopeless jumble resulted when listening with only one pickup whenever several conversations were going on simultaneously. In contrast, he states:

> With the binaural system, each party could be distinguished separately and it was fairly easy to understand everything that was said. [Moreover] . . . it was possible to understand speech under conditions of extremely high room noise. . . .

Finally, Koenig noted that very intense sounds were tolerable when heard with both ears. This "squelch" effect appears to be a further advantage of a binaural system.

Years ago both theoretical considerations and everyday observation led to the belief that binaural hearing aids should bring added benefit to many patients with auditory impairment. The prime requisite, according to this view, was that the impairment be one where bilateral stimulation was still possible. This belief, for example, lay back of the interest shown at the Psycho-Acoustic Laboratory, over a decade ago, in developing a prototype for a wearable instrument with two complete amplifying channels. Concurrently, both in military centers for aural rehabilitation and in civilian practice, sporadic attempts were being made to equip patients with two conventional aids. These patients were urged to employ dual amplification throughout the day. In such instances, the aids were selected from among the instruments currently available on the commercial market.

Such attempts almost always failed, even though it could be clearly demonstrated that auditory efficiency was enhanced when two aids were used. Most

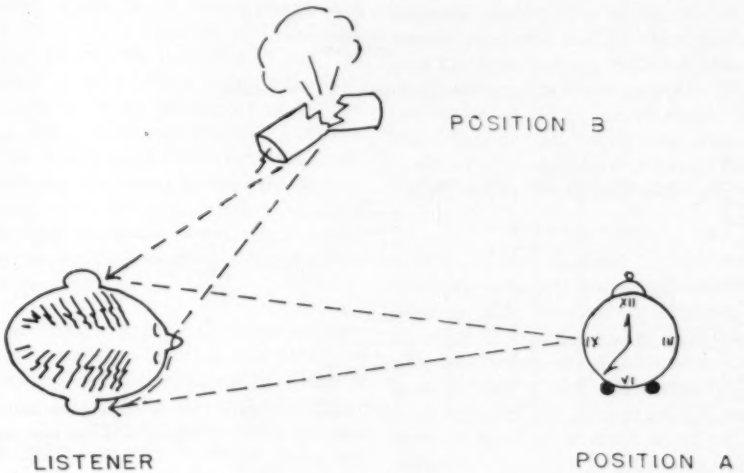

FIG. 1—Schematic diagram illustrating acoustic triangulation of sound sources.

wearers felt that the disadvantage of carrying two large aids on the chest outweighed the additional benefit in hearing which was gained. Thus, the only patients who could be induced to tolerate binaural fittings were those with particular need for maximum auditory efficiency.

The case reported in figure 2 relates to one such individual, who was supplied with a binaural hearing aid system in 1944. This man had lost his sight and much of his hearing in an explosion which occurred some months earlier. His unaided binaural loss for speech, as determined with spondaic words, was 66 decibels. This result was reasonable in view of the configuration of his pure tone audiogram. His residual loss while wearing a single instrument was 24 decibels for the left ear and 22 decibels for the right ear. His residual loss was only 10 decibels while wearing two instruments at the same time. Moreover, his ability to follow group conversations and to localize environmental sounds was infinitely better with two instruments. While wearing only one, for example, he could tell the direction a car was traveling only after it had passed. By contrast, with two aids he could determine, at 150 feet, the direction from which it was approaching. It is not necessary to emphasize the survival value which differences of this type have for a blind man. Needless to say, the patient wore both aids.

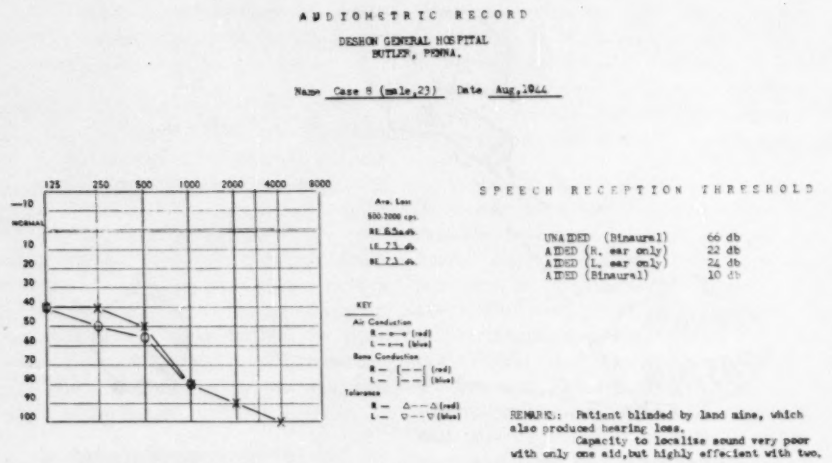

FIG. 2—Test results yielded by a patient with bilateral nerve deafness and illustrating extra benefit from a binaural hearing aid system.

Such examples were the exception. Moreover, there was no appreciable increase in the acceptance of binaural hearing aids as long as instruments had to be worn on the body. In view of the notable reductions in size which were achieved by the industry as years passed, one must therefore doubt whether the cumbersomeness of early instruments was the prime reason for the clinical failure of the binaural hearing aid. A more reasonable conclusion seems to be that there is a limitation to any binaural system which requires that the two aids be placed on the torso. The reason is probably to be found in the fact that no practical arrangement of the two instru-

ments on the body can place them in a sound field that reproduces the acoustic relations which exist at the two ears. For one thing, the general patterns of sound diffraction induced by the body are unlike those produced by the head. Secondly, the response of the hearing aid itself is changed by the so-called "body-baffle" effect.[3] This change is unpredictable because it depends on the dimensions of the instrument, upon the exact position where it is being worn, and upon the relative location of the sound source. In the third place, as long as practical considerations require that the two aids be worn on the front of the body, the contrast in acoustic patterns will be less than if full lateral positioning of the instruments were employed. Finally, if it were practical to employ such positioning the instruments would be separated by a much greater distance than the width of the head.

The foregoing limitations were overcome as soon as hearing aids were reduced in size to the degree at which it became feasible to wear them at ear level. Today many instruments of this type are available. Some of these instruments attach to the frames of glasses, other are cradled above and behind the auricle, while still others slip into the ear canal. They possess one critical feature in common; namely, the microphone which picks up the sound is in the immediate vicinity of the ear which the instrument activates. Two acoustic advantages are consequently achieved. First, the microphone now receives sound patterns which have been modified by the diffraction effects of the head rather than of the body. Second, when two units are employed to achieve binaural reception, their microphones constitute pickup points roughly equivalent to the two ears in their separation and their other physical relations. In consequence, many hard-of-hearing persons are now finding the practical benefits of the binaural system great enough both to overcome reticence against wearing two aids and to compensate for the extra cost of the second instrument. However, several limitations still restrict the usefulness of binaural hearing aids.

The first restriction is that instruments which can be easily worn at ear level are so small that they must be simple in construction. Circuity is uncomplicated, controllable variability of frequency response and of other performance features is not great, and behavioral characteristics are dictated in part by the rigor of space restrictions. Thus, these instruments serve best where the need is for straightforward amplification rather than for special electro-acoustic features.

Second, the clinician should remember that some of today's ultraminiature hearing aids possess unfortunate mechanical features, such as relatively exposed batteries, general flimsiness, awkward design of the volume control, and discomfort to the wearer. These factors need to be kept in mind when advising patients.

In the third place, the effective gain of the instrument is going to be limited by the onset of feedback. In other words, usable amplification cannot exceed the level at which the instrument begins to squeal because of self-excitation. Such feedback will ordinarily be acoustical. Acoustical feedback occurs more easily as the microphone is brought into closer proximity to the receiver and as sound radiating back to the microphone increases. The amount of such radiation often depends upon the snugness with which the earpiece fits into the auditory canal. However, excessive sound may be radiated directly from a poorly designed receiver. Occasionally, electrical feedback may be encountered. The important point is that, in binaural use, the

ear level hearing aid is capable of only moderate amounts of amplification before feedback is initiated.

Bearing the foregoing factors in mind, it is easy to see that there are many patients for whom the wearable binaural system is unsuitable. For one thing, the limitations on gain preclude its effective use by patients with severe losses. Again, it is difficult to achieve bilateral balance through binaural amplification when the two ears have highly asymmetrical audiograms. The same is true when the degree of loss is quite different in the two ears.

Conversely, many patients who exhibit moderate losses with reasonable bilateral balance receive benefits from a binaural system which a monaural aid cannot match. These benefits show themselves (1) through increased ability to cope with noisy situations, (2) through greater effective gain when the reception of faint sounds is critical, and (3) through a marked improvement in the precision of auditory orientation when the environment is complex. The child for whom these benefits can be achieved has both his educational progress and his social adjustment facilitated. The adult who experiences these benefits finds everyday life simplified. In extreme instances, the binaural system may effect dramatic restoration in efficiency. One hard-of-hearing physician, for example, was unable to find any monaural aid which allowed him to conduct his professional activities comfortably. He has been using a binaural system for the past two years. He is enthusiastic about the ease with which he can now deal with his patients, and he would not consider reverting to a single instrument.

The wearable binaural systems of today not only improve efficiency for many patients who can achieve substantial benefit from a monaural aid, they also make the use of amplification feasible for a large group of patients who do not obtain practical help from single-channel instruments. This group consists of people with mild losses whose two ears show reasonable bilateral equivalence of impairment. Many of these people find a monaural system more distracting than helpful except under the most uncomplicated listening situations. Yet these people often have the need to hear relatively faint material in less favorable, albeit not really noisy, circumstances. The enhanced capacity to establish figure-ground relationship which a binaural system allows often means successful hearing when otherwise difficulty and puzzlement would exist. The business executive with mild loss is one example. He often finds that with a binaural system it is much easier to follow the quick transitions from one speaker to another which characterize group conferences, directors' meetings, and the like. Similarly, the lawyer, the librarian, the teacher, and others may have their efficiency enhanced while performing professional tasks. Again, binaural hearing aids can provide significant benefit for many elderly persons whose mild presbycusic losses are not similarly helped by monaural aids. This benefit is experienced in group conversations, lectures, and the like. Remember that the phonemic regression which often accompanies presbycusis gives rise to auditory confusion. These confusions are multiplied by monaural amplification because such amplification disturbs the interaural balance in acoustic clues so necessary for the maintenance of the proper differentiation between foreground and background sounds. If an elderly person of this type is to benefit from amplification in those quieter situations in which he needs it, he must be given a hearing aid which does not trigger chaos in auditory perception. This requirement can often be met by a binaural instrument with good response characteristics.

The foregoing comments are generalizations. Unfortunately, awareness that wearable binaural systems can be of great help to many patients does not give the clinician the guidelines he needs in order to make specific decisions regarding the usefulness of such a system for a particular patient. Such decisions require two additional developments.

First, essential clinical criteria must be clarified through research. Our fields lack the knowledge necessary for intelligent prejudgment as to each patient's prospects for practical benefit from a binaural aid. Fortunately, some investigations in this area are underway, and the number can be expected to increase.

Second, since the final proof of a hearing aid's adequacy for a patient is the performance he achieves with it, the clinician must be able to gauge this performance directly. To this end, methods for appropriately testing a patient's efficiency with a binaural system must be refined and standardized. These methods must impose the rigor and acoustic complexity necessary to simulate the difficult listening situations of everyday life.

Two procedures which are currently used to assess efficiency of hearing aids fail to satisfy this last requirement.

The first one is the informal demonstration of instruments. Such an approach is too casual to give the information which is needed. Moreover, it lends itself either to conscious manipulation of conditions or to unconscious variation in the listening task, so that the relative merits of various fittings may be obscured. Finally, the listening task is usually kept so simple in demonstration situations that the results are meaningless as an indication of the performance the user may expect when auditory demands are exacting.

The second procedure which is inadequate for evaluating the binaural hearing aid is the formalized sound-field test administered through equipment with a single output channel. Such equipment is in widespread use because it is acceptable for assessing monaural instruments. Its limitation for use with binaural aids rests on the fact that competing signals cannot be initiated at different points in space if these signals must all travel through a common output stage. Obviously, the advantages of localization which binaural reception brings cannot be demonstrated when competing signals are all arising from the same spot. In recognition of this limitation, audiological facilities throughout the country are being improved either by adding second and fully independent channels to existing test instruments or by replacing these instruments with multichannel systems.

The full clinical potential of such multichannel equipment cannot be achieved, however, unless the tests administered through it are more complex than used heretofore in evaluation of hearing aids.* Such tests are in process of perfection in various centers, and standardized versions worthy of wide acceptance should emerge.

The fundamental requisite of such a test is that it explore the patient's capacity to perceive foreground and background relationships in the acoustic environment while wearing a binaural hearing aid. Thus, competing signals must be the critical feature of whatever new evaluative procedures are developed. Moreover, these signals must enter the test field from different points in space. One obvious version, which has been used by Markle,[2] is the measurement of discrimination for PB-50 materials when these are presented in noise. To

*Some of the tests which are currently employed, such as the measurement of aided threshold in quiet, will continue to be valuable. The point is that such tests cannot yield all the information requisite for evaluating binaural systems. Hence, since clinical procedures must be as brief as practical, appropriate substitution of new tests for current procedures is essential.

achieve a standardized test of this type it is necessary, of course, to specify the presentation level of the PB lists, the presentation level of the competing noise, the acoustic spectrum of the noise, and the physical relationships between sound sources and listener position. A second technique, which Wright has been refining at Northwestern University, is to bombard the patient with simultaneous samples of highly similar speech and to require that he attend to one of the competing trains of test items. A third alternative is one wherein the test material competes with itself, as occurs in everyday situations when reverberation and reflection of sound are severe. One simple procedure would be to reproduce each test item twice with only a small time delay between reproductions. This procedure may prove particularly critical in differentiating ability to follow connected speech with various hearing aid combinations. In any event, the tests which will emerge as clinically valuable in defining a patient's aided binaural efficiency will be those which are realistic in measuring his aided perceptual capacity under unfavorable acoustic circumstances.

SUMMARY

The usefulness of the binaural hearing aid will be more fully understood as research data and clinical experience accumulate. However, progress of critical importance has already occurred. Most notable is the development of instruments which can be worn approximately at ear level. With a binaural aid of this type, the listener's localizational skill allows him more easily to relegate momentarily unimportant sounds to the background of attention. However, improved equipment and new tests are needed if one is to guide patients most adequately regarding their individual prospects for practical success with a wearable binaural aid. Meanwhile, empirical trial has shown that present-day instruments can, through binaural fittings, bring enough added improvement to many persons with mild and with moderate losses so that their problems in everyday hearing are greatly simplified.

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DISCUSSION

SCOTT N. REGER, M.D., Iowa City, Iowa: Dr. Carhart's paper has presented the known factors pertinent to the use, abuse, limitations, and evaluations of the effectiveness of binaural hearing aids so completely that I find myself orally bankrupt. I agree wholeheartedly with everything Dr. Carhart has said, and I am somewhat chagrined by the fact that I am unable to contribute anything of significance to his paper; consequently I am reduced to a few brief anticlimactic remarks that are more or less self-evident.

A benefit that automatically accompanies the use of binaural eye-level hearing aids is the elimination of clothing friction noises which produce detrimental masking effects in the type of device that is worn under the clothing. A second advantage is the increase in directional perception which results from movement of the head while hearing binaurally at the eye level.

The psychological advantages of the eye-level aid, either unilateral or binaural, are fortuitous. Who among us ever convinced a patient who resisted the idea of wearing an aid that it was no worse to wear an instrument than a pair of glasses? Now we can say with the sincerity of an honest conviction that wearing a hearing aid is exactly the same thing as wearing eye glasses.

Any additional comment would be limited to expanding or emphasizing that which already has been stated adequately.

This situation reminds me of the story about a certain wise preacher of the gospel who, in spite of an obvious lack of formal education, had attained an enviable reputation as an effective speaker. When asked the secret of his success, he replied, "I has no secrets, but when I stands up in front of my congregation, first I tells 'em what I'se going to tell 'em; next, I tells 'em; then I tells 'em what I done told 'em."

VICTOR GOODHILL, M.D., Los Angeles: I have been waiting for such a paper for a long time. I fully realize that Dr. Carhart did not discover binaural hearing. However, this is the clearest exposition of the importance of binaural rehabilitation of the deafened individual to come to my attention. We are all aware of the part played by binaural messages in the localization of sound in space. The "third dimensional depth perception" of hearing is not only important in survival, as pointed out by Dr. Carhart, but also extremely important in the reception and intelligibility of speech. Let us not forget that elusive and difficult to measure element called "quality of hearing" or clarity, which patients experience so distinctly binaurally and miss so definitely monaurally.

The factors of *time of arrival* of acoustic messages, and *attention* have much to do with "listening" as a psychological function. Here also, binaural hearing plays a part.

We who deal with deaf patients daily and advise the use of hearing aids have not been unaware of the advantages of binaural hearing aids, yet the technical problems which are now being solved rapidly did prevent our suggesting such binaural aids routinely. There are still many practical problems in this field which the audiologists and engineers must solve. However, it is evident that there are a number of fairly urgent indications for the head-worn binaural aid, even in its present early form.

I consider as an urgent indication the case of the patient whose neural auditory lesion causes poor discrimination and precludes useful hearing with a monaural aid but does yield satisfactory discrimination with a binaural aid. May I cite the case of a young medical student with a bilateral sloping neural curve? His discrimination for speech with a monaural aid ranged from 32 per cent to 50 per cent. With a binaural aid his discrimination score jumped to 84 per cent.

The presbycusis patient who cannot wear any monaural aid will frequently (and surprisingly) accept with pleasure the hearing of a weak binaural aid, as mentioned by Dr. Carhart.

In evaluating binaural hearing aid performance, the multichannel technique employing a noise background has given us also a workable measurement of articulation scores in these cases.

I am quite sure that in a very short time most patients requiring amplification will receive it from the binaural aid. This is no more unusual than the choice of binocular glasses over the monocle, which has now been relegated to a quaint item in history.

Binaural hearing is also important in otologic surgery. When the fenestration operation first became available to otosclerotic patients, success so delighted the patients that both patients and otologists were content to obtain useful monaural hearing. With the passage of time, it became evident that this patient was having trouble in localizing the source of a sound. He still was confused in group conversation in identifying a speaker, and he still had the disadvantage of one deaf ear which invariably would be on the side next to an attractive young lady at the dinner table.

Accordingly, today otologic surgeons will usually recommend binaural surgical reconstruction in fenestration, stapes mobilization, and tympanoplasty in most cases. There are exceptional situations when such advice is contraindicated.

The psychologists will therefore be pleased to learn that those of us interested in restoration of hearing function are aware of the intricate central circuity of the auditory apparatus and that through either surgical or prosthetic methods we will attempt to give our deaf patients the use of two ears to deliver the third dimension of sound—a *very important faculty* and a real help to survival in a confused world.

KENNETH M. DAY, M.D., Pittsburgh: I guess you can call me exhibit X. I agree completely with Dr. Carhart's idea about binaural aids. The one thing that bothers me is clinical adaptation. I think you will find it quite difficult to persuade a harding-of-hearing subject to wear the aid in both ears. I have been trying for twenty years to get some of my patients to wear a hearing aid wired to both ears, the way I have worn one for twenty years. It has been only in the past two years that I have been able to wear two hearing aids. Before that, whenever I tried I would

get doubling of sounds because the aids would not synchronize. I need much amplification and cannot wear an aid close to my ears because of the feedback and squealing. I do very well with a hearing aid in my shirt pocket.

Several years ago I had my hearing analyzed at our Department of Audiology. I had 30 per cent discrimination in one ear and 20 per cent in the other. With a hearing aid wired to both ears, this improved to 48 per cent. This alone shows the added help that can be obtained by using both ears with which to hear. Two years ago I announced to my friends that it was the last Academy meeting I would attend because of my difficulty in understanding and because of excessive noise. However, since I have been wearing two separate aids I have been partially rehabilitated. For the first time in many years, music became pleasant, and I began to obtain depth perception. I still cannot get the direction of sounds very well, but the sense of depth and distance has been a tremendous help. I think the binaural aid will be especially helpful for individuals with excessive loss of hearing in both ears. In the minority who have disproportionate loss between the two ears, the binaural aid might not work.

The biggest difficulty in selling the binaural aid is connected with the artificially produced conductive deafness due to having both ears blocked. This causes distortion of the voice and it takes considerable time to modulate the voice properly. In this respect it might be helpful to start the patient off with a binaural aid and not give him the opportunity to wear an aid in one ear for a considerable time.

DR. CARHART: Let me say, first, that I am especially pleased that Dr. Day said the things he did. He pointed out much more adequately than I could the practical values of binaural hearing aids. In this connection, let me make this point clear. I would hate to have my earlier remarks interpreted as meaning that I do not believe that binaural amplification should be used by people with more severe hearing losses. However, there is a tremendous selling job to be done with many of these people. They are often resistant to the use of binaural instruments. One comes to the conclusion that the individuals with severe losses, since they cannot wear instruments easily on the head because of the feedback problem, must have special need for maximum amplification before they are willing to use binaural instruments.

One remark of Dr. Goodhill is especially valuable for us. He reminded us that we should be interested, not in binaural hearing aids, but in binaural hearing. He stressed that any system which will restore useful two-ear hearing to a patient who is hard of hearing is a very desirable thing. Obviously there are surgical or medical procedures which accomplish this goal.

I was especially pleased that Dr. Reger saw fit to point out that clothing noises, movements of the head for localization, and factors of that kind are eliminated.

FLOOR STAND MOUNTING FOR HIGH INTENSITY WOOD'S LIGHT

LESTER STEIN, M.D.
STEUBENVILLE, OHIO

THE use of the high intensity H100-SP4 General Electric mercury-arc lamp is facilitated by mounting the lamp and housing (as supplied commercially) upon suitable stands.

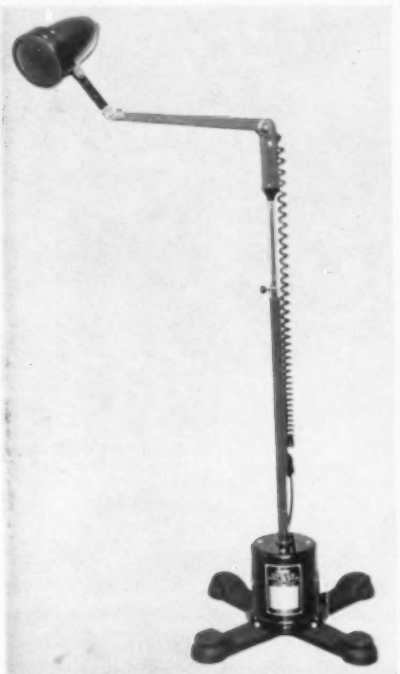

FIG. 1—Floor stand mounting for high intensity Wood's light.

The use of the Luxo adjustable bracket is described in my recent paper on Ophthalmoluminescence.[1] This floor stand model was fabricated* to permit more expeditious use of the hot lamp in the operating room and clinic, and for research purposes in photography of luminescent phenomena (photoluminography). The floor stand has an adjustable bracket, which can be raised and lowered, and can be mounted on caster wheels for movement (fig. 1).

Inasmuch as all mercury-arc lamps require a heating-up period for maximum flux, it is best to position the lamp near the operating table after all draping of the surgical field is completed. About ten minutes before expected use, the lamp should be turned on and swiveled away to prevent interference during the initial surgical procedures. In the event of need for the detection of lenticular residue after an extracapsular lens extraction, it is moved back into place. The white lights are extinguished and the operative field luminesced with the concentrated flux of Wood's light. The lamp is used quite readily for biomicroscopy or chair diagnosis and provides a safe method of utilizing the hot mercury-arc source.

*Burton Manufacturing Company, Colorado Avenue at 26th Street, Santa Monica, California.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

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NEW CIRCLINE FLUORESCENT TUBE PHOTOKERATOGRAPH

LESTER STEIN, M.D.
STEUBENVILLE, OHIO

PLACIDO's target disc of concentric circles is useful in revealing the tectonic nature and geometric curvature of the anterior corneal surface.[1] A photographic record or keratograph of the specular reflections of an illuminated pattern of circles provided the basis for the Zeiss-Amsler model of the keratoscope camera (no longer manufactured). The concentrically arranged triple circline fluorescent tube lighting fixture available commercially lends itself to the design of a simple keratograph (figs. 1 and 2). This type of electrical fixture is manufactured by several concerns and widely distributed. A triple circline fluorescent tube ceiling fixture, a direct focusing, axially mounted 35 mm. reflex camera, a standard chin rest and laboratory supports provide a serviceable photokeratograph suitable for general usage.

FIG. 1—Circline photokeratograph in use, showing integral chin rest and Jackson-Flexaframe supports.

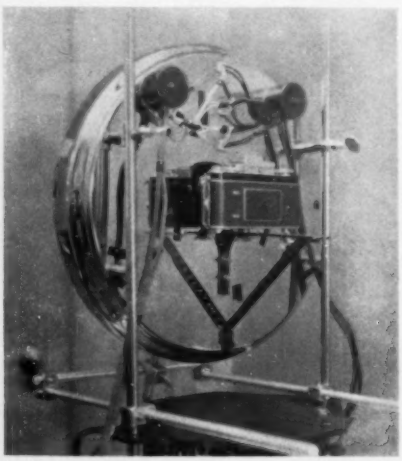

FIG. 2—Oblique rear view of photokeratograph showing method of supporting the housing on the Jackson lab stands and the Exakta camera support.

In keratoconus, cornea plana or keratoectasia, ulcerative or bullous keratitis, high-degree astigmia, and embedded foreign bodies, the deformation of the specular reflections of the luminous

Acknowledgment: The Medical Maintenance Shop personnel of the Walter Reed Army Hospital aided the mechanical construction and made valuable practical suggestions to simplify construction. Col. W. L. Spaulding (of the Eye Service) and Col. Austin Lowrey, Jr. (of the Ocular Research Unit) encouraged completion of the project while the author served as ophthalmologist of the 350th Evacuation Hospital in July 1956.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

Placido target is definitive and diagnostic. With regard to keratoplasty, Amsler[1] says:

> There is really only the Placido disc to reveal the initial state and successive phases of the adjustment of the graft to the form of the cornea, and also the degree of geometrical success of the keratoplasty.

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COMBINED WHITE AND BLACK LIGHT FLUORESCENT LAMP EXAMINING UNIT

LESTER STEIN, M.D.
STEUBENVILLE, OHIO

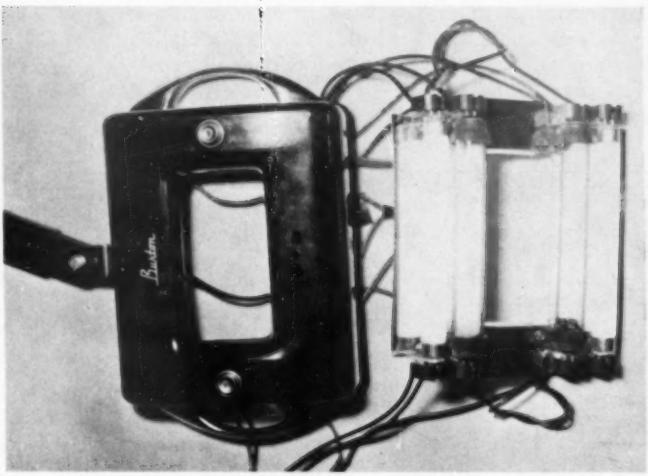

FIG. 1—Burton unit with one pair of black light and one pair of white light fluorescent tubes, showing both tubes illuminated, intricacies of wiring and two single-button Gaynor switches.

THE average luminescing unit, such as the Burton hand magnifier,* is now constructed with electrical circuits which can use only one pair of 4-watt fluorescent lamps at a time. It is difficult to change from white light to black light to provide rapid alternation of light for intensive study of luminescence of the ocular tissues.

Precancerous alteration of the tissues of the eye can be determined by studying

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

*Burton Mfg. Co., Colorado Ave. at 26th St., Santa Monica, Calif.

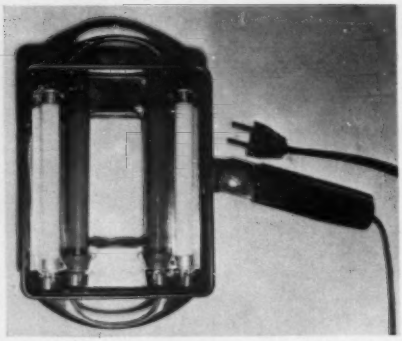

FIG. 2—Appearance of nonenergized fluorescent tubes showing positioning.

changes in luminescence of the anterior ocular segment and the ocular adnexae. A simple reconstruction of the Burton unit will provide an efficient method of incorporating and utilizing an extra set of miniature bi-pin sockets, ballast and switch so that a double pair of fluorescent lamps can be incorporated in the unit and alternation of white light and Wood's light is facilitated (figs. 1 and 2).

This setup permits rapid alternation of white light and black light flux without disturbing the mesopic state of the observer. After a few minutes of dark adaptation, light up the black light pair of lamps first and then, with the other hand on the white light button, illuminate the white light pair to catch quick glimpses alternating with black light luminescence. A binocular magnifier loupe for additional magnification is worn while peering through the magnifying lens. Mounting the unit on the Burton fleximatic support lends mobility for chair diagnosis.

AN INSTRUMENT FOR LAMELLAR KERATOPLASTY

J. H. KING, JR., M.D.
and
S. B. CHAVAN, M.D.
BY INVITATION
C. W. FURNESS
BY INVITATION
WASHINGTON, D. C.

IT is often necessary to dissect a lamellar graft from an excised donor cornea. Corneas preserved by dehydration in glycerin can be used with success equal to that obtained with fresh donor material, and these corneas are readily available for emergency application. It is more difficult to dissect the lamellar graft from an excised cornea. The cornea must be placed over a cork or a convex plastic button so that it can be fixed securely by pins as the trephine is applied and the graft is dissected (fig. 1).

A new instrument* resembling a chalazion clamp is useful for this pur-

From the Eye Research Section, Department of Surgery, Georgetown University Medical Center, Washington, D. C., and the Ocular Research Unit, Walter Reed Army Medical Center, Washington, D. C.

This investigation was supported in part by a research grant, B-975 (R), from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service, and by the Lions 22C Eye Bank and Research Foundation, Washington, D. C.

*Manufactured by Storz Instrument Company, St. Louis.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

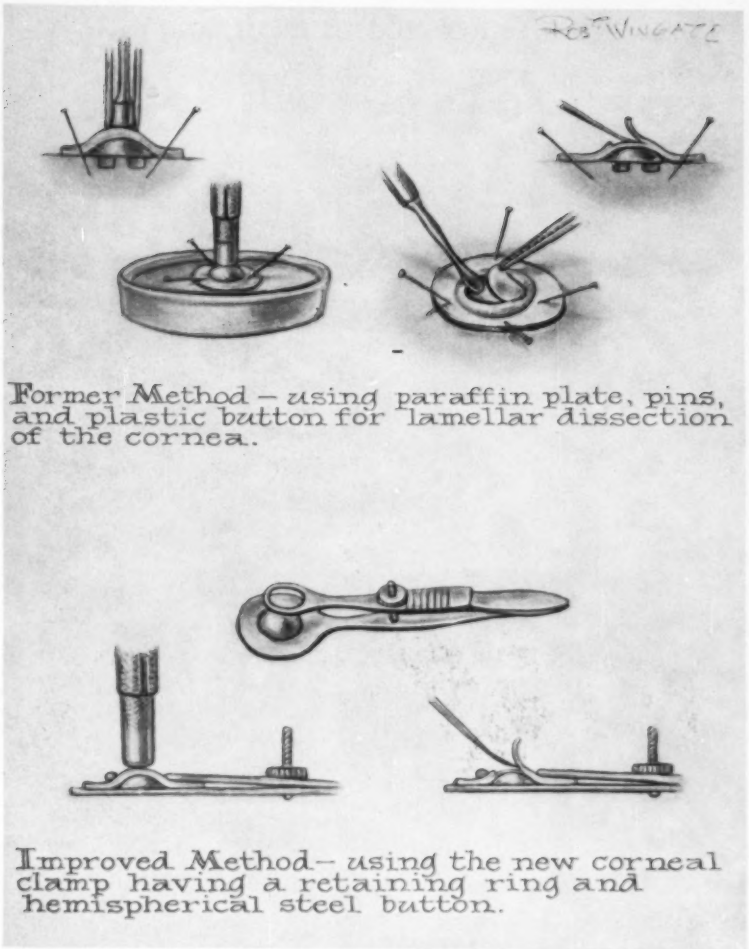
Former Method – using paraffin plate, pins, and plastic button for lamellar dissection of the cornea.
Improved Method– using the new corneal clamp having a retaining ring and hemispherical steel button.

FIGURE 1.

pose. The lower blade is convex, with its radius of curvature the same as that of the cornea. The upper blade is a circular ring and is made in two sizes, 8 mm. and 11 mm., the surgeon's choice depending upon the size of the lamellar graft to be excised. The ring slopes outward (on its inner surface) from above, down. The excised cornea is placed over the convex lower blade with the epithelial surface up. When the upper circular blade is closed and secured, the cornea is firmly fixed. The assistant steadies the instrument while the surgeon applies the trephine blade and completes the lamellar dissection in the usual manner.

HAND FUNDUS CAMERA

DAN M. GORDON, M.D.
NEW YORK, NEW YORK

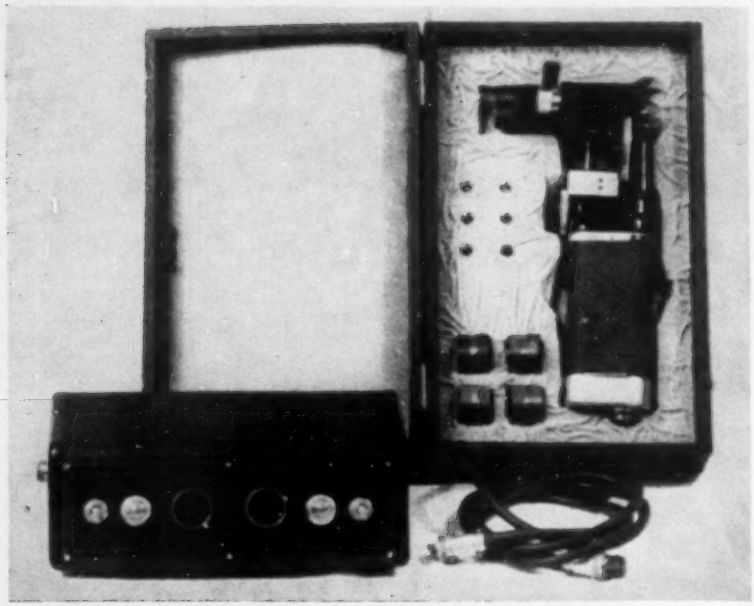

FIGURE 1.

DR. SATOSHI NOYORI has invented a portable fundus camera which combines the principles of a direct ophthalmoscope and a monoflex camera. The film size used is 16 mm., giving a picture much smaller than the Zeiss-type camera; if necessary, the picture can be easily enlarged.*

A Xenon electronic flashlamp (50 watt sec. in about 1/1000 sec.), powered by house current, is the light source.

This camera, which should be available in 1958, will simplify fundus photography considerably, making it an easier and less expensive procedure.

From New York Hospital-Cornell Medical Centre, 441 East 68th Street, New York.

*This camera is now being revised to use 35 mm. film.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

SMALL CURVED PROBE FOR BERMAN LOCATOR

JOHN P. WENDLAND, M.D.
MINNEAPOLIS, MINNESOTA

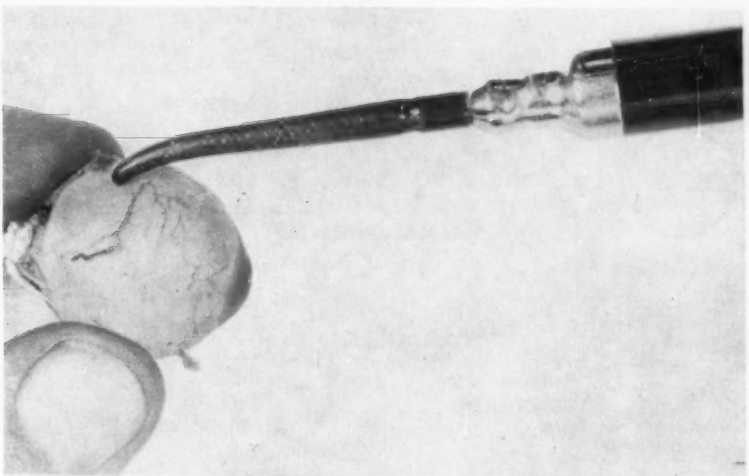

FIGURE 1.

THE Berman locator has proved helpful in detecting and locating intraocular foreign bodies. However, the probe available has been straight and large, making its use behind the equator of the eye difficult. A smaller, curved probe is therefore highly desirable. Engineering problems in the construction of a curved metal core and in the winding of such a core have been overcome, and a new probe for use in the eye has now been designed (fig. 1).

Since this probe is smaller than the original probe, some sacrifice in sensitivity had to be made. Our experience with the original probe indicated that this reduction in sensitivity could be done safely. The new probe* has 60 per cent of the sensitivity of the original probe and will detect magnetic foreign bodies from a distance of approximately six times their diameter.

We have been using only the new probe to locate intraocular foreign bodies, although it is conceivable that in a rare instance one might wish to use the straight probe first. Because the tip on the new probe is smaller in diameter, locating any magnetic intraocular foreign body is more precise. It is vastly superior to the old probe in locating foreign bodies posterior to the equator of the globe.

Maximum accuracy is obtained when the probe is perpendicular to the surface of the sclera. It should not be boiled or cold sterilized. Sterilizable, thin rubber jackets are available for it.

*Manufactured by Berman Laboratories, 112-03 Rockaway Blvd., Ozone Park 20, N. Y.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

A COLOR TELEVISION OPHTHALMOSCOPE

ALBERT M. POTTS, M.D.
CLEVELAND, OHIO
and
MURRAY C. BROWN, M.D.
BETHESDA, MARYLAND
BY INVITATION

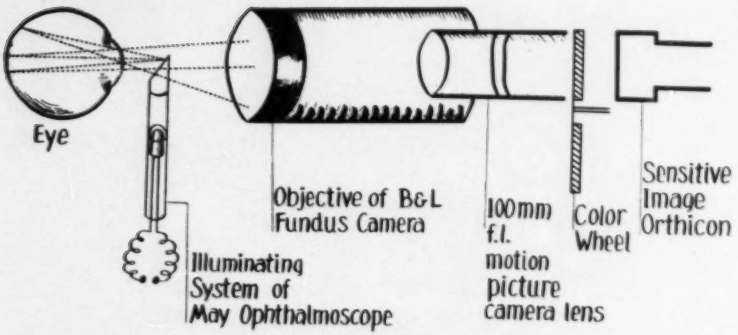

FIG. 1—Image tube TV ophthalmoscope.

THE production of an accurate color image of the fundus oculi on a television monitor screen is desirable for a number of reasons. None of these reasons has to do with routine physical examination, for which the hand ophthalmoscope is unchallenged. Perhaps the most obvious situation in which a color television image is useful is in the teaching of ophthalmoscopy. Simultaneous visibility to all in a large audience, the ability of the teacher to demonstrate the exact lesion under discussion, and the immediate availability of the patient for comparison with the direct ophthalmoscope are all highly desirable features.

A more remote but not unthinkable application is that of long distance consultation in which the fundus lesion of a patient may be viewed by a consultant physician many miles away.

In addition, color values may be purposely distorted to better demonstrate a particular lesion. The classical view with so-called "red-free light" may now be truly monochromatic, thanks to the availability of interference filters and the sensitivity of the television tube. Indeed, by color translation techniques, wave lengths in the ultraviolet and infrared invisible to the unaided eye may be utilized for examination and appear in color on the television screen.

In addition to these potential clinical applications there are a number of research applications which are of value. Using a series of monochromatic filters, one could actually measure the absorption spectrum of a lesion as an aid to categorizing it. By selecting a single line

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

electronically from the television picture, one can display blood vessel diameters as peaks and valleys on a cathode ray oscilloscope screen and record the dynamic changes in these dimensions on magnetic tape for later analysis. Thus vasospastic disease and the pharmacodynamics of vasomotor drugs may be studied with facility.

With the above considerations in mind, an apparatus was constructed by us to present a color television view of the ocular fundus (fig. 1). Illumination may be either by the May prism system shown or by zirconium arc through the objective lens of the ophthalmoscope. The high aperture rear lens of the optical system is an important feature of construction. The sensing device is a field-sequential (CBS) color camera chain.

The resultant image is bright enough to allow cinematography with fast color film. Resolution of the monitor image is surprisingly satisfactory but allows of some improvement. Further development of the apparatus as well as investigation of its applications is now under way.

RUBBER-TIPPED METAL APPLICATOR

JOSEPH E. ALFANO, M.D.
CHICAGO, ILLINOIS

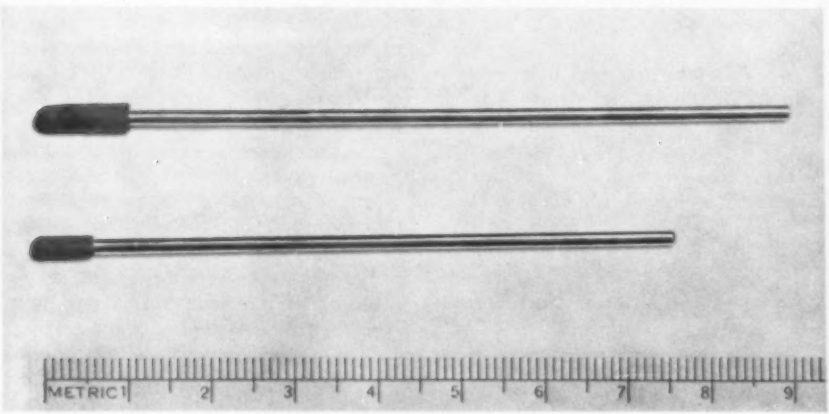

FIGURE 1.

SOME ophthalmic surgeons use a cotton applicator or cotton swab to retract or push aside the limbal based flap in cataract or glaucoma surgery. The rubber-tipped metal applicator (fig. 1) is preferable, since it averts the possibility that cotton fibrils may be left in the eye.

From the Department of Ophthalmology, Northwestern University Medical School, Chicago.

Presented as a *New Instrument* at the Sixty-Second Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 13-18, 1957, Chicago.

In Memoriam

Eldridge Stevens Adams.....Inglewood, California
December 9, 1957

William D. Black.....St. Louis, Missouri
December 2, 1957

Thomas Francis Gowen.....Corona Del Mar, California
October 19, 1957

Edwin A. Griffin.....Brooklyn, New York
December 29, 1957

William Henry Minton.....St. Joseph, Missouri
November 2, 1957

Fritz Nelson.....Colorado Springs, Colorado

Denis F. O'Connor.....South Orange, New Jersey
November 2, 1957

Sir John Herbert Parsons.....London, England
October 7, 1957

Isadore M. Shapero.....Rochester, New York
October 27, 1957

Everett Hale Tomb.....Framingham Centre, Massachusetts
October 25, 1957

Hugh C. Wolfe.....Greensboro, North Carolina
November 9, 1957

TRANSACTIONS

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All communications regarding the TRANSACTIONS should be addressed to
William L. Benedict, M.D., LL.D., Executive Secretary-Treasurer
American Academy of Ophthalmology and Otolaryngology
15 Second Street S.W., Rochester, Minnesota

FIELD INVESTIGATION: USE OF DIAGNOSTIC PROCEDURES AND THERAPY IN UVEITIS

The Council Advisory Committee on the Field Investigation Use of Diagnostic Procedures and Therapy in Uveitis (3-B-9023 [cl]) has been given the final information on assembly of the kits of antigens and the brochure on directions for their use. Since tests for toxoplasmosis, brucellosis and leptospirosis will be made in the Public Health Communicable Disease Center Laboratory in Chambley, Georgia, special forms for use by ophthalmologists who send serum for testing will be furnished by the Service. It is proposed to have mailing tubes supplied with the kits. Replacements will be made directly from the laboratory. It is not necessary for ophthalmologists who are engaged in this investigation to send sera for toxoplasma tests through the local Public Health Service. Full directions for use of the diagnostic antigens and comments on reading and reporting the results of the various tests will be included in the brochure of directions.

Preparation of the diagnostic kits is now underway, and it is the hope of the Committee that they will be ready by the first of May. Participation in the Field Investigation is anticipated from clinical centers where facilities for giving the tests and reporting the results are available. As many of the tests involve reading of skin tests, it is hoped that collaboration with allergists will be encouraged. There are still some problems to be solved. The feasibility of using disposable syringes is being looked into. The Committee feels that to begin with, patients with uveitis should be referred to a center where one technician makes the test and one ophthalmologist can supervise the investigation and follow the course of the response to therapy.

Diagnostic antigens will be sent free to ophthalmology clinics and hospitals for cooperation in the study. Requests for supplies of antigens for testing should be directed to the American Academy of Ophthalmology and Otolaryngology, 15 Second St. S. W., Rochester, Minnesota.

AWARDS FOR ORIGINAL INVESTIGATION IN OTOLARYNGOLOGY

Each year the American Academy of Ophthalmology and Otolaryngology offers awards for outstanding investigative work performed during residency training. These awards are an expression of the high value which the American Academy of Ophthalmology and Otolaryngology places on original effort as the basis of medical progress.

The main purpose of the awards is to give recognition for outstanding investigations performed by young physicians who have focused their attention on Otolaryngology. The Academy also hopes that the award program will provide an extra stimulus for those who have investigative ideas as well as a stimulus to department heads to provide time and facilities so that their students can pursue these ideas.

Separate awards will be given for clinical and for basic investigations in the broad field of Otolaryngology. The broad field of Otolaryngology includes the ear, nose, throat, nasopharynx, oral cavity, larynx, esophagus, tracheobronchial tree and neck. Clinical investigation is understood to mean any study involving human patients which contributes information regarding the symptomatology, etiology, diagnosis, course, complications, therapy, etc., of any otolaryngological disorder. Basic investigation includes any study which involves histological, physiological, audiological, experimental-surgical and other similar procedures or lines of investigation. Research may be both of the clinical and of the basic types, such as a study involving both humans and animals, and the Awards Committee will decide in which category such a manuscript is to be considered.

The competition is open to Doctors of Medicine who have completed at least one year of internship (not necessarily in the United States or Canada) and who began resident training in Otolaryngology no longer than five years past. Residency training must be in an approved American or Canadian hospital but the contestant need not be an American or Canadian citizen. The investigative work must have begun during the normal three or four year residency program but may be completed afterward. The majority of the investigative work must have been performed by the contestant, although he may acquire needed advice and technical assistance. The work need not be entirely original and may represent a continuation of research already in progress in a laboratory. The author's name should appear on the title page. Co-authors may be listed, but the contestant must be the first author. When an equal contribution to the investigation has been made by two or more qualified contestants, a letter should accompany the manuscript stating this fact. A cash award made for an entry having two or more qualified authors will be divided equally between these authors.

The Academy wishes to allow the contestant complete freedom in the publication of the manuscript. Thus, both published and unpublished papers will receive equal attention so long as they are submitted within the time limitations indicated. Reprints will be accepted, if submitted within one year of publication. Manuscripts must be typewritten and follow accepted style for journal publication. An accompanying letter should state whether the manuscript has been published or has been submitted for publication.

Judgments of merit will be based on scientific content as well as the manner of presentation. Manuscripts should contain a minimum of historical detail, review of the literature and statements of opinion.

The manuscripts must be in the hands of the Secretary of the Subcommittee on Research of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology not later than October 1, 1958, for awards to be presented in October 1959.

Awards will be made at the discretion of the Committee on Research and Finance of the Council of the American Academy of Ophthalmology and Otolaryngology and may be withheld if there are no manuscripts of merit. Cash awards shall not exceed six in number and shall not total more than $5000.00 in any one year. The award may be made for either clinical or basic research. Certificates of Merit may be awarded for exceptional manuscripts not winning cash awards. Letters in support of manuscripts will not be accepted by the Awards Committee.

At the discretion of the Awards Committee, one or two of the first award papers may be recommended for presentation at the annual meeting of the Academy.

HAROLD F. SCHUKNECHT, M.D.
Sec'y, Subcommittee on Research,
Committee on Conservation of
Hearing, American Academy of
Ophthalmology and Otolaryngology

Special Report

EVALUATION OF THE "PHOSPHENATOR" DEVICE FOR THE DETECTION OF INCREASED INTRAOCULAR TENSION

LEONARD T. KURLAND, M.D.

F. STERLING DAVIS, JR., U. S. ARMY, M.C.

and

DAVID SACHS

BY INVITATION

LARRY C. KERPELMAN

BY INVITATION

WASHINGTON, D. C.

ACCORDING to recent reports by Humphrey and Murgolo,[3,4] application, for a few seconds, of a low voltage, low amperage electric current to the skin bitemporally just behind the eyes "will excite the optic end organs so that a bluish-white phosphene (light sensation) is observed by the normal eye, while in the case of increased intraocular pressure the patient reports yellow, orange, or red phosphenes." The test is easily and rapidly performed, and "it is not necessary to contact the eye at any time."[3] The advertisement and the brochure which accompanies the Phosphenator device manufactured by the Hausted Company of Medina, Ohio, state that this is a "new electronic instrument for the rapid diagnosis of glaucoma and macular and peripheral loss of vision."[1]

Since glaucoma is a major ophthalmologic problem in the older population, a method of glaucoma detection which is accurate, simple, and atraumatic would be of obvious advantage. The present investigation was undertaken to determine the validity and reliability of the Phosphenator in selecting individuals with increased intraocular tension and in identifying persons known to have glaucoma.

METHOD

One hundred and ninety-five male subjects from various wards in the U. S. Soldiers' Home Hospital (USSHH) and 27 male and 22 female subjects at the Walter Reed Army Hospital (WRAH) were examined. The median age of the USSHH group was 72 years; that of the WRAH group was 61 years. There were several Negro patients in each group.

The USSHH group consisted largely of elderly patients whose hospitalization was not necessarily related to any ophthalmologic complaint. On the other hand, 36 of the 49 WRAH subjects had glaucoma*; the others were normal sub-

Dr. Kurland is Chief, Epidemiology Branch, National Institute of Neurological Diseases and Blindness (NINDB), National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare, Bethesda, Md.

Dr. Davis is Chief, Ophthalmology Research Unit, Walter Reed Army Hospital, Washington, D. C.

David Sachs and Larry C. Kerpelman are student employes in the Epidemiology Branch and the Biometrics Branch, respectively, NINDB.

*The diagnosis of glaucoma on the patients included here had been made after thorough study at the WRAH Ophthalmology Department. The diagnosis was reached after routine ophthalmologic examinations as well as the following tests:

jects or patients with conditions other than glaucoma. The intraocular tension of the glaucoma patients was well controlled by miotics, by surgical intervention, or by both, in 23 of the 36 patients.† Tension fluctuated or was difficult to control in the other patients with glaucoma.

The subjects at both the USSHH and WRAH were tested by a member of the investigative team, using a Phosphenator which was supplied by Dr. Carroll E. Humphrey. The testings were conducted in accordance with the directions in the Phosphenator brochure[1] and after preliminary instruction by Dr. Humphrey. Following a standard pretest introduction, the subject's responses to standard testing questions were recorded for each eye. The following questions were asked: (a) What do you see? (If no response, Do you see a flickering?) (b) If affirmative, What color is the flickering light in each eye? (c) Select the color from the chart which corresponds closest to the color you saw during the test. The standard color chart prepared by Dr. Humphrey has eight color discs: (1) white, (2) pale blue, (3) pale yellow, (4) bright yellow, (5 and 6) shades of orange, (7 and 8) shades of red. According to Dr. Humphrey, color responses 1, 2, and 3 are "normal," colors 4 to 8 are "abnormal responses, indicating increased intraocular tension."[2,3]

Each subject was then tested for color blindness and color comprehension by a member of the investigative team using standard Ishihara color cards. The USSHH subjects were then examined independently by two members of the investigative team, each using a standardized Schiøtz tonometer. The WRAH group included many patients who had had extensive ophthalmologic studies previously, and a single tonometer reading was taken shortly after the Phosphenator and Ishihara tests were carried out for the subjects in that group.

It should be stressed that in every instance the results of the Phosphenator, Ishihara, and tonometer tests were known only to that member of the investigative team who administered the particular test. No information relating to the condition of the eyes was obtained from any of the subjects prior to the recording of the test results.

Results of the various tests were combined for each subject and appropriate statistical evaluations were then carried out.

RESULTS

Most of the subjects in both the USSHH and WRAH groups responded to the Phosphenator tests in the "expected" manner, that is, they gave a straightforward description of the flickering and the color and selected a color from the chart which corresponded to the description. Many other subjects either described a color which was not compatible with that which they selected from the chart, insisted they saw nothing, or were unable to select any color from the chart. Thus, the subjects were categorized, on the basis of these factors, into three groups:

1. Acceptable (A)—The subjective description of the color sensation produced by the Phosphenator stimulus was in agreement with the color chosen from the color chart.
2. Questionable (Q) — The subject was undecided and altered his

1. Repeated tests of tension with different weights on different days
2. Visual field examinations
3. Provocative water tests
4. Gonioscopy
5. Where indicated, electrotonography

†The 36 glaucoma patients had been classified as follows: open angle, 24; narrow angle, 7; secondary, 5.

TABLE I

CLASSIFICATION OF PATIENTS BY TYPE OF RESPONSE TO PHOSPHENATOR TEST

CATEGORY OF RESPONSE	USSHH		WRAH	
	NUMBER	PER CENT	NUMBER	PER CENT
Acceptable	128	66	43	88
Questionable	21	11	3	6
Unreliable	46	23	3	6
Total	195	100	49	100

choice of color, with or without repetition of the Phosphenator stimulus.

3. Unreliable (U)—The subject was unable to describe what he observed or there was gross inconsistency in the subject's response.

The categorization of responses for the subjects in both groups is presented in table 1. The percentage of acceptable replies was appreciably lower in the USSHH group, which included many very elderly and debilitated individuals. It is clear that even a simple test such as the Phosphenator has some limitations for population surveys if it requires comprehension of even elementary directions and a description of a subjective experience.

The "acceptable" (A) subjects were then divided, on the basis of the Ishihara test results, into two groups: color normal (N) and color defective (D). The group whose response to the Ishihara test was unsatisfactory included individuals with poor comprehension of the test as well as color blindness. Thirty-five of the 128 subjects in the A class of the USSHH group and 9 of the 43 subjects in the A class of the WRAH group were found to be color defective.

Statistical analysis of the results of the Phosphenator test and tonometer reading were then made for the 95 AN ("acceptable" and normal Ishihara test result) subjects at the USSHH and the 34 AN subjects of the WRAH group. The patient's color selection for each eye following the Phosphenator stimulus was plotted against the corresponding tonometer reading. For the USSHH group, the average of the two tonometer readings was taken, since these independent readings were found to agree very well in almost every instance.

The results of the tonometric examination of 185 eyes for the USSHH group are summarized in table II. In 19 eyes (10.3 per cent), the average tension was greater than 25 mm. Hg. *In only one of these 19, however, was the*

TABLE II

TONOMETER READING VERSUS COLOR CHART SELECTION FOLLOWING PHOSPHENATOR STIMULUS FOR EACH OF 185 EYES OF 93 AN PATIENTS AT USSHH

AVERAGE TONOMETER READING (MM. HG)	PHOSPHENATOR COLOR RESPONSES		
	NORMAL	ABNORMAL	TOTAL
0-24	161	5	166
25 and over	18	1	19
Total	179	6	185

TABLE III

TONOMETER READING VERSUS COLOR CHART SELECTION FOLLOWING PHOSPHENATOR STIMULUS FOR EACH OF 67 EYES OF 34 AN PATIENTS AT WRAH

TONOMETER READING (MM. HG)	PHOSPHENATOR COLOR RESPONSE		
	NORMAL	ABNORMAL	TOTAL
0-24	51	2	53
25 and over	14	0	14
Total	65	2	67

Phosphenator response abnormal. In 7 eyes the tension was greater than 30 mm. Hg, but in all these the Phosphenator response was the "normal" blue or white. On the other hand, an "abnormal" color response was reported for 6 eyes, but in only one of these was the tension suspiciously high. Re-examination several weeks later of the subjects with either abnormal Phosphenator responses or increased tension failed to affect these results materially.*

On the basis of this analysis, it would appear that the Phosphenator results cannot be depended upon to differentiate subjects with increased tension from those with normal tension.

In the 65 AN eyes of the WRAH group, there were 14 (21.5 per cent) with tension above 25 mm. Hg. *In none of these was the Phosphenator color response "abnormal"* (table III). Only one patient in the AN group gave an abnormal Phosphenator response. This patient, a 67-year-old man, had chronic open angle glaucoma. A left iridencleisis four years previously and 2 per cent pilocarpine four times a day in the right eye had controlled the intraocular tension, which on the day of this examination was 12 mm. in the left eye and 17 mm. in the right eye.

Of the remaining 33 AN patients, *all of whom gave a normal Phosphenator response,* 10 were controls and did not have glaucoma and 23 were patients of the glaucoma clinic of the WRAH.

Of these 23 glaucoma patients, 20 had wide angle glaucoma, 1 had narrow angle glaucoma, and 2 had secondary glaucoma. Tension was well controlled in most cases with miotics, with surgical intervention, or with both. However, tension was greater than 30 mm. Hg in one patient with a secondary glaucoma and in 3 patients with wide angle glaucoma; tension was between 25 and 30 mm. Hg in 6 other patients with wide angle glaucoma, and in 1 other patient with secondary glaucoma. In each of these cases with an elevated tension, the Phosphenator responses were normal and equal in the two eyes, even when the tension was elevated in one eye only.

On the basis of this analysis, we find the Phosphenator cannot be relied upon to identify glaucoma patients whether their tensions at the time of the examination are elevated or not.

The results of the comparison of intraocular tension and the Phosphenator response for the two groups are sum-

*Of the 7 subjects with an abnormal Phosphenator response and normal tension, 6 were still found to have tensions well within normal limits; their ophthalmological examinations were negative in all other respects. One of the 7 had a tension of 26 mm. Hg in one eye, but results of his examination were otherwise normal.

Thirteen of the 16 subjects (19 eyes) with suspicious or increased tension were re-examined for glaucoma. Seven were found to have chronic open angle glaucoma; 5 were newly diagnosed cases resulting from these tonometry studies; 1 was considered borderline and suspicious; and 5 were found to have normal tensions and no other evidence of glaucoma.

TABLE IV

TONOMETER READING VERSUS COLOR CHART SELECTION FOLLOWING PHOSPHENATOR STIMULUS FOR EACH OF 252 EYES OF 127 AN SUBJECTS AT USSHH AND WRAH

TONOMETER READING (MM. HG)	PHOSPHENATOR COLOR RESPONSE		PERCENTAGE ABNORMAL	
	NORMAL	ABNORMAL		
0-19	133	4	2.9	
20-24	79	3	3.7	
25-29	21	1	4.5	3.0
30 and over	11	0	0.0	
Total	244	8	3.3	

marized in table IV. The over-all frequency of an "abnormal" Phosphenator response was 3.3 per cent. There was no difference in the frequency of the abnormal Phosphenator response with respect to intraocular tension.

Further correlations by age, sex or race fail to add to these disappointing results. It might be stated that for the 44 AD subjects ("acceptable" but Ishihara defective individuals) there was one patient with increased tension who had a normal Phosphenator color response; in this same group there were 13 "abnormal" Phosphenator responses, but in all of these the tension was less than 25 mm. Hg. Seven of this AD group were patients from the WRAH glaucoma clinic; all but one of the 7 had given a normal response to the Phosphenator test.

Although a tonometer reading above 25 mm. Hg is believed to represent a suspiciously high intraocular tension, it can be seen from table IV that selection of 20 mm. or even 30 mm. Hg as the point of increased tension gave the same unsatisfactory results for the Phosphenator test.

COMMENT

This study fails to show that the Hausted Phosphenator, as developed by Dr. Humphrey, is of value in detecting increased intraocular tension. This conclusion holds whether the arbitrary selection of normal intraocular tension is 20, 25 or 30 mm. Hg. The Phosphenator test provided equally poor results in locating subjects with increased intraocular tension in the USSHH group and in identifying patients of the WRAH glaucoma clinic.

An appreciable number of subjects failed to give an acceptable color response when tested with the Phosphenator stimulus. Some of these were senile, but many elderly subjects who were otherwise well oriented and cooperative could not describe the effect of the stimulus. This emphasizes the need for a screening device for glaucoma which is less dependent upon a subjective response.

In passing, it might be pointed out that in contrast to the report by Humphrey and Murgolo,[2] we found it difficult to evaluate the field of vision with the Phosphenator device.

There were very few complaints of discomfort when the stimulus was applied, and, to our knowledge, the Phosphenator test is harmless.

Although in our hands the Phosphenator test had no merit as a means of identifying persons with increased intraocular tension, further study might

seem worth while to determine why a few of those tested reported observing yellow, orange, or red phosphenes.

SUMMARY

The Phosphenator developed by Humphrey and now being widely advertised and marketed for the "rapid diagnosis of glaucoma" was evaluated in a study of 195 elderly veterans at the U. S. Soldiers' Home Hospital and 49 patients and employes at the Walter Reed Army Hospital. Individuals who gave a poor response to the Ishihara color test and those who could not give a reliable response to the Phosphenator test were not included in the statistical evaluation. The tonometer and Phosphenator results are presented for 93 USSHH patients (185 eyes) and 34 WRAH patients and employes (67 eyes). The Phosphenator results failed to differentiate individuals with low or suspiciously high intraocular tensions. The Phosphenator response was "abnormal" in 7 of the 219 eyes (3.2 per cent for the USSHH and WRAH groups combined) with tension under 25 mm. Hg and in 1 of 33 eyes (3.0 per cent) with a tension above 25 mm. Hg. In 32 of the 33 eyes with high or suspiciously high tension, a normal response to the Phosphenator stimulus was obtained. In the WRAH group, the Phosphenator was not a reliable means of differentiating the normal subjects from glaucoma patients whether the tensions in the patients were well controlled or not at the time of the examination. In individuals wtih uniocular increased tension, there was no difference in the Phosphenator response for the two eyes.

CONCLUSIONS

The Phosphenator was found to be of no value in detecting increased intraocular tension. Our results have failed to substantiate the claim that the device has merit in the diagnosis of glaucoma, since it failed to provide a reliable means of identifying known glaucoma patients. We believe there is a potential danger in the use of this apparatus because it may give a false sense of security regarding the absence of glaucoma to individuals tested by this device alone.

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1. Instructions for using the Phosphenator, a new, electronic instrument for the rapid diagnosis of glaucoma and macular and peripheral loss of vision. The Hausted Manufacturing Co., Medina, Ohio.
2. Humphrey, Carroll E.: Personal communication.
3. Humphrey, Carroll E. and Murgolo, V. J.: A simple and rapid test for glaucoma, EENT Monthly, 36:106-107 (Feb.) 1957.
4. ———: The use of phosphenes in detecting visual loss, EENT Monthly, 36:170 (March) 1957.

INTERNATIONAL ASSOCIATION OF SECRETARIES OF OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETIES

Minutes of Annual Meeting October 15, 1957

The Eighteenth Annual Meeting of the International Association of Secretaries of Ophthalmological and Otolaryngological Societies was held at the Palmer House in Chicago at 5:30 p.m., Tuesday, October 15, 1957, in conjunction with the annual convention of the American Academy of Ophthalmology and Otolaryngology, the Association being the dinner guests of the Academy.

On the preceding October 12, a committee, appointed to work with Dr. William John Holmes toward the organization of the Asia-Pacific Academy of Ophthalmology, consisting of Drs. Edley H. Jones, chairman, Moacyr Alvaro, Paul Craig, Dan DeStio, Archie Cruthirds and Col. Austin Lowrey, M.C., held a meeting. On October 13 the executive board held a meeting, with all members in attendance. On October 14 the Council held a luncheon meeting, attended by President A. E. Cruthirds, President-elect Dan DeStio, editor Paul Craig, directors Moacyr Alvaro, Harry Glick, Ricardo Fernandez, Lewis Morrison, Roland Myers, and Ernest I. Glenister (representing Dr. Viger), executive board members Willard Goff and Roderick MacDonald, and secretary Edley H. Jones. Their actions and recommendations were referred to the Association and are incorporated in the following minutes.

During the dinner a register was signed by all attending. Following the dinner, President Cruthirds called the meeting to order and called on each one present to introduce himself and indicate the Society he represented.

MINUTES OF PRECEDING MEETING

Since the minutes of the last meeting had been distributed to each secretary, and had been printed in the TRANSACTIONS of the American Academy of Ophthalmology and Otolaryngology, it was moved that they not be read but approved as printed. The motion was seconded and unanimously carried.

PRESIDENT'S REPORT

The president distributed a typewritten report (attached to and incorporated in these minutes), supplementing it with a few remarks describing his trip through the Orient and his contact with ophthalmologists in Oriental countries.

SECRETARY-TREASURER'S REPORT

The secretary reported the actions of the executive board in electing Dr. F. E. Murdock an active director to succeed Dr. Dan DeStio, president-elect; and electing Dr. Jesus V. Tamesis of Manila a cooperative director. The secretary further reported that, as of October 1, 1957, there were 67 paid active fellows, 3 paid associate fellows and 2 honorary fellows; and that there was a cash balance in the treasury of $1,097.87.

The secretary read a letter from Dr. Jorge Balza of Buenos Aires regretting he could not attend. He also reported many notes on cards from foreign directors expressing their regret at not being able to attend and sending their greetings to those present.

Editor Paul Craig reported that the Academy has continued to allot the Association four pages in each issue, and thanked the membership for aiding him in furnishing copy.

The president then called for committee reports.

VI INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

Dr. Paul Holinger reported that the VI International Congress of Otolaryngology was by far the best attended and most successful one held; and thanked the Association for its assistance, and for serving as host at a hospitality lounge for foreign visitors during the Congress.

ASIA-PACIFIC ACADEMY OF OPHTHALMOLOGY

The president then called on the secretary for a report on the Asia-Pacific Academy of Ophthalmology. The secretary explained that Dr. Holmes was unable to attend the Academy meeting because his presence was required at a meeting in San Francisco in November and he could not attend two meetings in this country held so close together. No attempt was made to review the voluminous correspondence, but the secretary reported that much progress had been made and that the ophthalmologists in the Asian-Pacific countries were definitely interested. The secretary then read the report of the committee (described above), which had been approved by the executive board and by the council, and the latter body recommended adoption by the Association:

The committee recommends that the International Association of Secretaries of Ophthalmological and Otolaryngological Societies:

Congratulate Dr. William John Holmes on his wonderful work.

Commend him for the interest he has aroused among ophthalmologists in the Asia-Pacific area.

Express full appreciation of his spirit of cooperation and willingness to aid the organization of the proposed Academy in any capacity.

Request Dr. Jesus V. Tamesis to further the organization by requesting the selection of a representative from organized groups in each country to work toward the perfection of the organization.

Suggest considering the desirability of organizing the otolaryngologists as well as the ophthalmologists, which may require a representative of each group in each country.

Suggest that, when such a group is selected, they plan a meeting at which time officers can be elected and rules of organization can be adopted.

Recommend that ophthalmologists from the western hemisphere attending the International Congress of Ophthalmology in Brussels in 1958 return via the Orient to promote friendly international contacts; and aid in arranging schedules for those who do, and are willing to address meetings of interested ophthalmologists.

INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

Dr. Moacyr Alvaro then reported on the work of the International Council of Ophthalmology. He stated that the Asia-Pacific Academy of Ophthalmology was considered a *fait accompli*. He discussed the progress made by the Council in improving teaching in ophthalmology in the various countries. He closed by stating that he felt that this Association was now entitled to a seat on the Council.

GOOD-WILL AMBASSADOR

Dr. Sam H. Sanders, who had been appointed a good-will ambassador by the Association on his recent trip to Europe, reported a warm and friendly reception during his visit, and that continental groups were interested in the work of this Association.

AUDITING COMMITTEE

The auditing committee, composed of Drs. Lewis E. Morrison, chairman, J. David Stratton and Roland H. Myers, reported that it had reviewed the financial records of the Association and had found them neatly and correctly kept, and in perfect order, with a cash balance of $1,097.87. The committee report was accepted and approved by motion, duly seconded and unanimously carried.

NOMINATING COMMITTEE

The president then called on the nom-

inating committee and Dr. Paul Craig, chairman, made the following nominations:

For president, Dr. Dan S. DeStio; for president-elect, Dr. Roland H. Myers; for secretary-treasurer, Dr. Edley H. Jones; for editor, Dr. Paul Craig; for active director (for 3 years), District 1, Dr. M. H. Barone (to succeed himself); District 4, Dr. Fred R. Guilford; and for District 6, Dr. Harry Glick (to succeed himself).

The committee report was accepted by motion, duly seconded and unanimously carried. The president announced that, at the end of the meeting, he would call for further nominations from the floor and the election would then be held.

CERTIFICATE OF MEMBERSHIP

Under the heading of old business, the secretary read a letter from Dr. Peter Pastore suggesting that members of this Association be provided a certificate of membership. Dr. Pastore supplemented the letter by stating that this might arouse more interest among the individual members and suggested that if the total cost were too much for the treasury, those secretaries who desire a certificate would individually pay for their own certificate. Dr. Stratton moved that the matter be tabled until next year, and that the president appoint a committee to study the matter and report at the next meeting. The motion was seconded and discussion followed. Dr. Murdock suggested that a receipt be furnished each member which would serve as a certificate of membership. Dr. Craft urged that secretaries serve as long as possible; and that the Association give them a certificate after they serve five years. Dr. Pastore then suggested that a questionnaire be sent to the individual members. The discussion was closed and the motion was carried.

AID FOR QUALIFIED FOREIGN STUDENTS

At the last meeting, the Association approved the plan of aiding qualified foreign students to attain residencies in ophthalmology and otolaryngology in this country and some effort had been devoted to this matter during the past year. The council had discussed the matter quite thoroughly and recommended that the function of the Association in this matter be to provide information to the applicant — not to obtain the residency — the applicant to deal directly with the institution providing the residency; and that, to facilitate matters, two committees be appointed, one for ophthalmological students, with Archie Cruthirds as chairman, and the other for otolaryngological students, with Willard F. Goff as chairman, the chairmen to select the personnel of their committees. This action was approved by motion duly seconded and unanimously carried.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY

Under the heading of new business, the secretary read a letter from Dr. Filippi-Babardi suggesting that those officers and directors of this Association attending the International Congress of Ophthalmology in Brussels in 1958 hold a meeting during the Congress. It was moved, seconded and unanimously carried that such a meeting be held.

Dr. Paul Craig then stated that this Association was entitled to a delegate to the International Congress and moved that Dr. Archie E. Cruthirds be elected delegate. His motion was seconded by Dr. Lewis Morrison and unanimously carried.

HONORARY FELLOWSHIP

The president then called on Dr. Paul Craig to make a presentation. After a few appropriate remarks, Dr. Craig presented Dr. Moacyr Alvaro a certificate of honorary fellowship in this Association, with the enthusiastic applause of

those present. Dr. Alvaro modestly accepted and expressed his appreciation, followed by more applause.

ELECTION OF OFFICERS

The president then called for further nominations for officers and directors from the floor. There were none, and the above listed nominees were elected by acclamation.

The secretary then called the Association's attention to the matter of additional directors, reporting that the council had recommended that there be two active directors from Canada, one from the eastern area and one from the western area; that Dr. Cooper had suggested that another be elected from India to represent the otolaryngologists; that Dr. Cruthirds had reported that there were 4,000 ophthalmologists and 4,000 otolaryngologists in Japan, and that an additional cooperative director should represent the Japanese otolaryngologists; and that Prof. J. Francois, secretary general of the European Society of Ophthalmology, had suggested a director from their membership. The hour was late and it was moved, seconded and unanimously carried that the executive board be authorized to redistrict Canada; elect a new director from Canada; and create and fill such cooperative directorships as are indicated.

There being no further business, the meeting adjourned.

EDLEY H. JONES, M.D.
Secretary

President's Report for 1956-57

IV INTERIM CONGRESS OF PAN-AMERICAN OPHTHALMOLOGICAL ASSOCIATION WITH THE NATIONAL SOCIETY FOR PREVENTION OF BLINDNESS

The meeting was held in New York City in April 1957. We cooperated in every possible way to provide publicity among ophthalmological societies.

SIXTH INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

This meeting was held in Washington, D. C., in May 1957. Our Association served as host at a Hospitality Lounge for Foreign Visitors. Shortly before the Congress convened, Lederle International of American Cyanamid offered to serve as co-host, Lederle "picking up the check." While that was nice, it was even nicer that several of their representatives who could speak foreign languages were in attendance. Drs. Goff, DeStio, and Edley Jones and I were there most of the time. We were delighted with the charming manner of the Lederle representatives as they made our foreign guests feel at home. Of course we did our best, too.

EXCHANGE OF PROGRAMS AND PROGRAM PLANNING

This Association embraces local, sectional, state, regional, national and international groups. One of our objectives is the improvement of programs for all groups. Would it be of interest to secretaries of the same group of societies to exchange programs? This is one of the matters we have had under consideration, and if you feel that such an exchange of programs would be beneficial, please write to the secretary.

NEWS AND EDITORIALS

Dr. Benedict has graciously continued to give us space in the TRANSACTIONS of the American Academy of Ophthalmology and Otolaryngology. We have published pertinent editorials and information. Please send your programs and other news to our Editor, Dr. Paul C. Craig, 232 North Fifth St., Reading, Pa.

FOREIGN RESIDENTS

Last year Dr. William John Holmes of Honolulu and others suggested that this Association could aid qualified foreign physicians to obtain residency train-

ing in this country. Three applications were received during the year. They are under consideration.

ASIA-PACIFIC ACADEMY OF OPHTHALMOLOGY

Last year this Association authorized Dr. William John Holmes of Honolulu to study the possibilities and perhaps begin the organization of such an Academy.

It was a fortunate coincidence that I had already planned a world tour. In India my wife and I were honored by being the guests of Dr. and Mrs. Sorab Cooper. While attending the All-India Ophthalmological Society I enthusiastically endorsed the Asia-Pacific Academy of Ophthalmology. We had a very enjoyable visit in Manila as the guests of the Philippine Society, thanks to Dr. Jesus Tamesis and the Ocampos (husband and wife). There I also found much interest in an APAO.

In Hong Kong we found the local society in favor. In Japan I was more than amazed to find well organized groups totalling more than 4,000 ophthalmologists and 4,000 otolaryngologists, entirely separate specialist groups. The Japanese, too, were enthusiastic about an APAO.

Dr. Tamesis of Manila was particularly and articulately interested in the APAO. He was recently in the United States as an invited scientific speaker. While here he honored me with a visit and also visited with Colonel Lowrey in Washington. Dr. Tamesis made certain suggestions which he thought essential to the formation of the APAO; for instance, he suggested that it should be an Asia-Pacific Academy of Ophthalmology *and* Otolaryngology. All of his suggestions are under study by our Board and Council and by a special committee.

During the past year the Executive Board has been a "working team." We believe we have accomplished certain things. What we have done is the result of a pooling of all of our efforts. I want to thank particularly the past president, Willard Goff; the incoming president, Dan DeStio; the editor, Paul Craig; an executive board member, Rod MacDonald; and, most of all, our secretary, Edley Jones, for their aid, encouragement and assistance.

There is no question about the desirability, yea, the necessity of worldwide understanding and cooperation. As American ophthalmologists and otolaryngologists we have a major responsibility, commensurate with our advantages and enjoyment, to do everything we can for international friendship. If we hope to gain friendship, we must not turn our potential friends into mere recipients. We must not talk down to them and make them feel that they are inferior. They definitely are not! We have very much to gain from mutual relations. The free exchange of ideas and information and the building of confidence should be our gift to foreign physicians. They are proud, and justly so, of what they have accomplished under considerable difficulties. They have shown courage, patience, ingenuity, skill and knowledge. They have much to teach us, perhaps more than we can do in return. If we can make this clear to ourselves, we will create a long-term feeling of friendliness rather than a sensation of doubtful gratitude. Let us build better cooperation with our foreign colleagues.

My term of office was a challenge and an opportunity. I have enjoyed my work for the secretaries of eye, ear, nose and throat societies, and I feel that my understanding of our country's good-neighbor policy has been immeasurably enriched.

ARCHIE CRUTHIRDS
President

News - - - Notes

ALLERGY CONGRESS

The Third International Congress of Allergy will convene in Paris, October 19-26, sponsored by the International Association of Allergology and the French Allergy Association. The program will include symposia on asthma and emphysema, immunology, recent clinical advances, biochemical aspects, autoimmune reactions, dermatology and socio-economic aspects. Short sectional papers will be given on all phases of allergy.

The registration fee for allergists attending the Congress is $32.00; the fee for a relative is $15.00. For further information about the program or papers write Samuel M. Feinberg, M.D., 303 E. Chicago Ave., Chicago, or, if you are in Latin America, write Jose M. Quintero Fossas, M.D., Paseo 313, Vedado, Havana, Cuba. In all other countries, and for information about and registration for the Congress, write Bernard N. Halpern, M.D., 197 Boulevard St. Germain, Paris 7.

OPHTHALMOLOGICAL CONGRESS

The 43rd Annual Meeting of the Oxford Ophthalmological Congress will be held July 7-9, 1958, in the Lecture Hall of the School of Physiology, South Parks Road, Oxford, England. The topics to be discussed are "The Early Clinical Diagnosis of Glaucoma," "The Aetiology and Treatment of Uveitis," and "The Influence of Vascular Changes in Progressive Failure of Vision."

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY SOUTHERN SECTION

Call For Papers

The 1958 meeting of the Southern Section of the Association for Research in Ophthalmology will be held in New Orleans, November 11, conjointly with the Eye, Ear, Nose and Throat Section of the Southern Medical Association.

If you wish to present a paper before the Southern Section, contact A. E. Meisenbach, Jr., M.D., Secretary, Southern Section, Association for Research in Ophthalmology, 317 Medical Arts Bldg., Dallas 1.

An abstract of 75 words or less is required for publication in the official bulletin of the Southern Medical Association. A second abstract, no word limit, can be submitted for publication in the Research Section of the American Journal of Ophthalmology. The 75 word abstract must arrive by July 1, in order to meet the deadline set by the Southern Medical Association.

SPECIAL PROGRAM IN ST. LOUIS

A special one day program will be presented by the Department of Ophthalmology of the Saint Louis University School of Medicine, March 27, in honor of the twenty-fifth anniversary of its main teaching hospital, Firmin Desloge Hospital in St. Louis. Ophthalmologists throughout the country are especially invited to attend the program free of charge. It will be held in Miller Hall of the hospital.

Dr. Bernard Becker, professor of ophthalmology at Washington University, will speak about "The Role of Electrotonography in the Management of Glaucoma"; Dr. V. Everett Kinsey, assistant director of research at the Kresge Eye Institute in Detroit, will discuss "Lens Metabolism in Normal and Diabetic Animals"; and Dr. Paul A. Chandler, associate professor of clinical ophthalmology at Harvard University, will discuss "Practical Considerations in the Management of Narrow Angle Glaucoma."

One more guest, as yet unannounced, will speak, and Dr. Elmer J. Ballintine, senior instructor in the ophthalmology division, department of surgery, at Western Reserve, will be the guest speaker at the evening dinner meeting of the St. Louis Ophthalmological Society, which will conclude the session. Luncheon at Desloge Hospital will be provided free of charge. Send reservations to William H. Vogt, Jr., M.D., Chairman, Desloge Jubilee Committee, 1325 South Grand, St. Louis 4.

LARYNGOLOGY AWARD

The Gould Award, this year $250.00, will be given by the William and Harriet Gould Foundation of Chicago to a recipient selected by an international committee of laryngologists. The Award is presented for outstanding research in laryngology in order to encourage and reward fundamental investigations in this field. While it is given in recognition of the completion of a specific research project, favorable attention will be given to investigators with a long-term interest in this subject.

For further information, contact the nearest member of the committee: Sir Victor Negus, 149 Harley St., London, W.1; Prof. Cotohi Satta, M.D., No. 111 Morikawacho, Bunkyo-ku, Tokyo; Prof. Dr. Eelco Huizinga, Academisch Ziekenhuis, Afd. Keel-Neus-Oorheelkunde, Groningen, The Netherlands; or Hans von Leden, M.D., Medical Director, William and Harriet Gould Foundation, 30 N. Michigan Ave., Chicago 2.

PUGET SOUND ACADEMY OFFICERS

Dr. Willard Goff is the new president-elect of the Puget Sound Academy of Ophthalmology and Otolaryngology. Elections were held at the annual President's Meeting, January 11. Dr. James L. Hargis was elected secretary-treasurer and Dr. George Drumheller was elected trustee.

During the meeting, Dr. Lester G. Jones lectured on the lacrimal apparatus. Five new members were given certificates of fellowship in the Academy. At the close of the meeting the retiring president, Dr. E. DeMar Anderson, presented the gavel to the incoming president, Dr. Edison G. Dorland.

SCHOOL OF OPHTHALMOLOGY— CUBA

The Foundation for the Teaching and Advancement of Ophthalmology (F. E. D. O.) announces that registration opened January 1 for the course for specialists in the diseases of the eyes. Applications must be received before March 31 and the chosen applicants must be in Havana, Cuba, the day before the course begins (June 2).

Dr. Tomas R. Yanes will direct the studies, with the cooperation of the professional body of the League Against Blindness. The classes, theoretical and practical, will be held in the hospital of the Institution. The two-year course is correlated with the program of the School of Ophthalmology.

The number of first year students is limited to ten doctors selected from the Latin American countries. They must hold the degree of doctor of medicine, be at least 35 years old and have been out of medical school no more than five years, and have acceptable moral qualifications.

The cost of the course is $500.00 (Cuban) each year, payable $250.00 each semester in advance. The students will have to take care of the cost of food, lodging and miscellaneous expense, as well as travel. Student loans are available.

Additional information can be secured from the Senior Director of the F.E.D.O., Liga Contra la Ceguera, Calzada de Columbia 7601, Marianao, Havana, Cuba.

IRISH OPHTHALMOLOGICAL SOCIETY

The Irish Ophthalmological Society will hold its meeting in Dublin, May 1-3, 1958. The Montgomery Lecture will be given by Prof. Dr. A. Hagedoorn of Amsterdam in Trinity College, Dublin, on Thursday, May 1.

POSITIONS AVAILABLE

RESIDENCY AVAILABLE

A two year residency is available in ophthalmology. The physician will be trained in general ophthalmology with special oportunities in ophthalmic plastic surgery. This salaried position will begin September 1, 1958, at the Hempstead General Hospital in Hempstead, N. Y. For information contact Wendell L. Hughes, M.D., 131 Fulton Ave., Hempstead, N. Y.

OPHTHALMOLOGIST

An ophthalmologist, Board certified or eligible for Board examination, is wanted to take over the practice of the late Dr. Fritz Nelson. The practice is 20 years old and includes an office with excellent equipment and library. The office is located in a residential area with ample parking space. For further information write to Mrs. Fritz Nelson, 1121 N. Tejon, Colorado Springs, Colo.

Listings of positions available should be sent to W. L. Benedict, M.D., 15 Second Street S.W., Rochester, Minn., by the fifth of the month preceding publication. They should include (1) type of physician wanted (ophthalmologist or otolaryngologist: diplomate, resident, etc.); (2) type of position to be filled; and (3) whom to write for further information. Unless otherwise requested, listings will be published only once.

The Academy will handle no further correspondence beyond the listing and assume no responsibility. Neither does it endorse nor guarantee any of the published listings.

BOOK REVIEWS

MANAGEMENT OF COMPLICATIONS IN EYE SURGERY: AVOIDANCE OF PITFALLS AND TREATMENT OF DIFFICULT SITUATIONS IN OPHTHALMOLOGIC OPERATIONS. Edited by R. M. Fasanella, M.D., Chairman of the Section on Ophthalmology, Yale University School of Medicine. 422 pp. Illustrated. $16.00. Published by W. B. Saunders Company, Philadelphia.

Designed to serve as a reference book, this volume of papers by twenty-three distinguished authors takes the place of reprints, journals, and texts on subjects that are of concern to the ophthalmic surgeon. Most chapters deal wtih complications in operative procedures that may not occur in the practice of an individual enough times for him to be mindful of the circumstances in which they may develop and of the precautions that may be taken to avoid them. For the most part every chapter, each of which deals with a separate subject, is written by an ophthalmic surgeon whose name is associated with the subject in current literature. Stress is placed on the avoidance of pitfalls. It makes good reading for any eye surgeon, and he can profit from it by perusing the pertinent chapters before beginning the day's surgical clinic.

The book is well printed and illustrated adequately. It is a very valuable reference book.

SURGERY OF THE HEAD AND NECK TUMORS. By Hayes Martin, M.D., attending surgeon at Memorial Hospital; Associate Professor of Clinical Surgery, Cornell University Medical College, New York. Cloth. $18.50. 430 pp., 599 illustrations. Published by Paul B. Hoeber, Inc., 49 East 33rd St., New York 16.

This book is primarily addressed to the general surgeon, since it is the opinion of the author that this type of surgery requires a thorough training in general surgery. This is in agreement with a rising

sentiment of the American Board of Otolaryngology, whose requirements for certification now include at least one year of residency in general surgery on an operative level. Otolaryngology has long felt the need for further training in general surgery to cope with the problems arising in neck resections, laryngectomies and removal of oral and pharyngeal tumors. Brain tumors are universally relegated to the neurosurgeon.

A comprehensive description of operations for all anatomic anomalies of the head and neck with the exception of brain tumors and eye tumors, is profusely illustrated by drawings, many of which are of operations originating in the Head and Neck Service of the Memorial Hospital. The surgical specialties of otolaryngology, ophthalmology and plastic surgery have their surgical divisions that care for superficial lesions as minor surgery. Dental surgeons are gradually encroaching on the field hitherto divided between the general surgeon and the otolaryngologist, and now there are at least five surgical specialties overlapping the field. This volume covers for all of them. Nearly all the described operations are currently in use, some fully accepted, others still on trial and under modification. The scope is comprehensive in deep lesions and scanty in superficial ones. There is not much for the ophthalmologist. The first one hundred pages are devoted to historical notes, preoperative considerations, anesthesia, technical considerations and cosmetic and functional disabilities. The balance of the book is an atlas of surgical drawings with explanatory text. General surgeons who operate in this head and neck region and the more recently trained otolaryngologist will refer to this volume as a classic in the field.

THE PHARMACOLOGIC PRINCIPLES OF MEDICAL PRACTICE. By John C. Krantz, Jr., Professor of Pharmacology, School of Medicine, University of Maryland, and C. Jelleff Carr, Senior Research Pharmacologist, National Institute of Mental Health, former Professor of Pharmacology, Purdue University, and Professor of Pharmacology, School of Medicine, University of Maryland. Cloth. $14.00. 1,285 pp., with full index and illustrations (some in color), portraits, cuts, diagrams and tables. Published by the Williams & Wilkins Company, Mount Royal and Guilford Avenues, Baltimore 2.

This is the fourth edition of a well-known text on the *Principles of Medical Practice* since the first printing in 1949. Changes made include addition of new material, especially one chapter on Local Use of Drugs in the Ear, Eye, Nose and Throat, expansion and rearrangement of former chapters for the better alignment of therapeutic agents with the fields of their greatest use. There are nine parts, each one embracing a field of therapeutic interest according to systems. The origin of drugs, their preparation and mode of dispensing and use are briefly covered in each part—more completely in some sections than others. The part devoted to Ear, Eye, Nose and Throat covers a few external inflammations and a list of commonly used local preparations in eye, ear, nose and throat practice. This list is already half obsolete and contains few of the currently used drugs. The *Principles* are classic and very good reading. A comprehensive reference book of practical value in every physician's office library.

W. L. B.

TEACHING AIDS

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ABSTRACTS

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